DR. A. S. WARTHIN.


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## CONTENTS


**THE MASSACHUSETTS MEDICAL SOCIETY**

SECTION OF PEDIATRICS

Serums and Vaccines in the Prevention and Treatment of Infectious Diseases—A Critical Review. *Benjamin White*..... 505

Autolysis of the Spleen. *Seth M. Fitchet, Lawrence Weld Smith*, and *Aubrey C. Benjamin*. 521

Agranulocytic Angina — Report of a Case with Recovery. *Tyree C. Wyatt*..... 525

A Contribution to the Study of Women in Medicine. *Kate Campbell Hurd-Mead*..... 527

**CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL**

Case 14301—Cough, Fever and Dyspnea Fatal in Three Days. *Richard C. Cabot.* Case 14302—The Value of Definite Localization of Abdominal Tenderness in Acute Upper Abdominal Pain. *Daniel Fiske Jones*..... 535

**EDITORIALS**

Trying It on the Consumptive..... 539

Lee Prefers Its Milk Raw..... 539

*The Commonhealth*..... 540

This Week's Issue..... 540


*(Contents continued on next page)*


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# CONTENTS

*(Continued)*

BOOK REVIEW
Strabismus, Its Etiology and Treatment. Oscar Wilkinson ..... 546
BOOKS RECEIVED FOR REVIEW ..... 546
BOSTON MEDICAL LIBRARY
Boston Medical History Club ..... 541
CORRESPONDENCE
The Norfolk District Medical Society. F. S. Cruickshank ..... 542
MISCELLANY
"Trench Mouth", or Vincent's Infection ..... 534
Virgil Pendleton Gibney Memorial Fellowship of the Hospital for Ruptured and Crippled. 541
The World's Children ..... 542
RECENT DEATHS ..... 542
REPORTS AND NOTICES OF MEETINGS ..... 542
SOCIETY MEETINGS ..... 545

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The New England
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## The Massachusetts Medical Society

### SECTION OF PEDIATRICS

TUESDAY MORNING, JUNE 5, 1928

THE Section of Pediatrics of the Massachusetts Medical Society, held in the Large Dining Room, Hotel Bancroft, Worcester, Massachusetts, convened at nine-thirty o'clock, Dr. Kenneth D. Blackfan, of Brookline, the Chairman, presiding.

CHAIRMAN BLACKFAN: Within recent years the number of so-called specific biologic agents for the prevention and treatment of disease has increased so remarkably that we thought it might be of value to have reviewed at this meeting the present-day views concerning the evidence on which the use of these agents is based. We feel very fortunate to have with us Dr. White, whom you all know, as he can speak authoritatively on this subject, not only from the point of view of the experimental work in the laboratory, but from the broader laboratory point of view, that is the bedside. Dr. White will present a critical review of serums and vaccines in the treatment of diseases of children.

### SERUMS AND VACCINES IN THE PREVENTION AND TREATMENT OF INFECTIOUS DISEASES — A CRITICAL REVIEW*

BY BENJAMIN WHITE, PH.D.†

THE medical practitioner is presented with an increasing array of serums and vaccines, and unless he be specially trained in immunology it is difficult if not impossible for him to ascertain their true value from the publications of their discoverers, from the claims of their exploiters or even from the experience of his fellow physicians. The discoverer may be not without prejudice, the exploiter oftentimes is surely not without bias, and the user of these biologic agents, unless his experience includes properly controlled observations, may in his reports be influenced by enthusiasm or lack of it, as the case may be, rather than by coldly critical judgment. The charge may also be made that the immunologist, if he is not at the same time a clinician, views the field of biologic therapy with a too limited vision. The immunologist, however, who is preparing and testing serums and vaccines acquires an intimate acquaintance with their chemical composition, their immunizing properties and their physiologic action in the animal body, and unless he be mentally shortsighted he will supplement his experience with the results of the actual use of these products in the prevention and treatment of communicable diseases. Here, even at the risk of being charged with pessimism, he must demand that clinical observations, if they are to be accepted, be made with the same care and accuracy and with the same rigid controls required in any scientific study. A critical review of biologic products should, therefore, be based on theoretical considerations and experimental data as well as on accurate observations of their use in practice. The present discussion will be from such a viewpoint and is limited to those serums and vaccines that concern the infectious diseases prevalent in this region.

1. *Anterior poliomyelitis.* Although the cause of this malady has not yet been isolated, the situation was never so promising as it is now. The fact that the disease can be transferred to monkeys opens the way not only for a study of the virus and the disease processes it elicits, but it gives us a means for measuring the preventive or curative action of biologic or other agents. Aycock has shown that by vaccination it is possible to immunize monkeys actively against this infection, but the method is not yet practical for application to humans. On the other hand, both laboratory and clinical experience would seem to show that the serum from persons convalescent from poliomyelitis has neutralizing properties for the virus and exerts an inhibitive and curative action on the infection when administered in sufficient quantity early in the infection. Theoretically, the shorter the time between the drawing of the blood and the recovery from the acute stage of the infection, the more potent should

*From the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Public Health.

Read before the Section of Pediatrics at the Annual Meeting of the Massachusetts Medical Society held at Worcester, Mass., on June 5, 1928.

†For record and address of author see "This Week's Issue," page 540.

be the protective power of the serum, although blood taken years after convalescence may still have curative value. The serum is separated from the cellular elements of the blood by the usual serologic methods, and tested for sterility. While the dosage is still arbitrary it is customary to inject about 15 to 20 cubic centimeters of this convalescent serum intraspinally and about double the amount intravenously. Other serums advocated for the treatment of this disease have been found by some investigators to have little or no protective or neutralizing action on the virus, so on theoretical, experimental and clinical grounds convalescent serum as yet remains the most promising biologic agent for the treatment of this disease.

2. *Anthrax.* Infections with the anthrax bacillus are relatively uncommon, but may be prevalent in localities where there is much traffic in wool and hides. Inasmuch as this infection may attack not only the skin but also the lungs and alimentary tract, many of the latter cases are beyond aid from surgical treatment. There is now procurable an anti-anthrax serum made by immunizing horses against virulent cultures. This serum, in the hands of Regan and others, has been found to have curative action, both alone or as an adjunct to surgical measures and should be given in all cases of this nature.

3. *Common Colds.* Until an answer can be found to the question, "What are common colds?" we cannot expect to devise any rational plan for biologic control of these infections. Many varied infections of the respiratory tract are classed under this convenient and inclusive term and in none of them have we more than an inkling of the causative factor. To be sure, the practitioner is offered a number of bacterial vaccines made up of those bacteria commonly isolated from infections of the nose, throat, trachea and bronchi. These organisms may be normal inhabitants of the mucosa of the buccal cavity and the respiratory tract or they may be the cause of secondary infection invading tissues already depleted by some other virus or its products. Here then is the only reasonable basis for their use, but from a theoretical standpoint little is to be expected of their immunizing action. In the case of pneumococci any immunity they produce is at best transitory, and in the case of some of the other bacteria included in the combined vaccines, if they produce any immunity it is generally specific for the individual strain injected. Yet clinical experience seems to show that where no pathologic lesions or abnormalities of the respiratory tract exist, the use of such vaccines may either prevent colds in persons chronically susceptible to such infections or at least mitigate their effects. They apparently are harmless and are worth further trial and more careful study.

4. *Diphtheria.* In this disease we have a full complement of reliable biologic agents for the determination of susceptibility, for the production of active immunity and for treatment. The Schick test when carefully performed with proper material is the same reliable procedure that it always has been. There is a possible technical error of two per cent. or less, but this does not seriously detract from its worth. The materials for the test must be fresh, they must be kept continuously cold until used, and injected precisely according to the detailed directions accompanying each outfit.

The diphtheria toxin-antitoxin mixture has undergone a series of modifications and the one-tenth L plus mixture is now the preparation usually used in this country. It gives a minimum number of reactions and is practically as good an immunizing mixture as the previous, more concentrated mixtures. The dosage should be exactly one cubic centimeter at each injection (except in persons over ten who show a combined reaction to the Schick test, when the first two or three doses should be less). The injection should always be made subcutaneously, and a Schick test should be given to every one six months after receiving the toxin-antitoxin injections. The number of persons rendered Schick negative by one series of three injections will vary with the immunizing strength of the particular preparation given and with the diphtheria history of the community in which the persons injected have lived. During the past year in some localities the percentage of negative reactors six months after toxin-antitoxin treatment has been disappointingly low, but preparations of considerably higher immunizing value are now available. It should be borne in mind, however, that as diphtheria decreases it may be increasingly difficult to immunize susceptibles, and lower percentages of those successfully immunized are to be expected.

There has been frequent discussion of the substitution of a modified toxin, such as Ramon's "anatoxine" or toxoid for toxin-antitoxin mixture. Such preparations have been released as satisfactory after laboratory study, and while they possess high immunizing value, their use, because of the reactions they cause, is limited to children, especially those below the age of six or seven. With improvements in their preparation it is probable that toxoids will in time supplant our present toxin-antitoxin mixtures. One toxoid, that prepared with sodium ricinoleate, has proved to be unsuitable for general manufacture and distribution.

The objection has been raised that toxin-antitoxin mixtures containing antitoxin derived from horse serum, may sensitize the person so that a subsequent injection of any serum or antitoxin of equine origin may cause uncomfortable, dangerous or even fatal reactions. There is no doubt that the injection of such toxin-antitoxin mixtures does set up a condition of hypersensitiveness to horse serum proteins in an appreciable number of those so injected but the condition apparently is not so serious as some report-

ers believe. Such sensitized persons may, to be sure, suffer in greater numbers than normal persons from serum sickness, sometimes in accelerated and aggravated form, after a subsequent injection of antitoxin or other horse serum product, but it is debatable whether it is advisable to replace horse antitoxin with goat antitoxin as some immunologists have recommended. In this regard, toxoid would be preferable to the present toxin-antitoxin mixtures.

Diphtheria antitoxin still is the most notable of antitoxins. Improvements in the method of concentration give a product of greater and more lasting potency and clarity and a reduced content of non-antitoxic serum proteins. The present day preparations make possible high unit dosage in small volume and their use is followed by a gratifying decrease in the number and severity of cases of serum sickness, so that this complication is now negligible. The rule of subcutaneous injections for prophylaxis, intramuscular for mild and moderately severe cases, with intramuscular and intravenous injections in severe cases still holds, and the curative effect will depend upon administration at the earliest possible moment and in sufficient amount. With the increased concentration and, therefore, decreased volume of present day preparations the full doses recommended by manufacturers should always be given.

5. *Encephalitis lethargica.* There is no accepted specific biologic agent either for the prevention or treatment of this disease, and neither does convalescent serum seem to be of any avail. Rosenow, who claims that a streptococcus may be the etiologic factor, has obtained an immune serum against this organism and has used it with signs of improvement in the cases treated. His work has not been confirmed.

6. *Erysipelas.* The work of Amoss, Birkhaug, Dochez and Stevens, and Williams indicates that hemolytic streptococci are intimately associated with this type of infection. This organism, or rather group of organisms, like their near relatives—the scarlatinal streptococci—produces a toxin, and against this toxin an antitoxin has been obtained and concentrated, which apparently has therapeutic value and is to be recommended in cases of this kind. Being an antitoxic serum its effects are mainly against the existing toxemia and it is not to be counted on to establish an active immunity against subsequent infection or recurrence.

The close relationship which apparently exists between erysipelas streptococci and scarlet fever streptococci would suggest the possibility of cross neutralization of the two toxins by the two antitoxins. There is already experimental evidence to show that this cross or reciprocal neutralization takes place, and, hence, it is reasonable to suppose that a potent scarlet fever antitoxin might exert detoxifying and curative action in cases of erysipelas. In the few such clinical tests as have been made this supposition is substantiated. It is, therefore, well worth the trial to administer scarlet fever streptococcus antitoxin to patients suffering from erysipelas if no erysipelas antitoxin is available.

7. *Gas Gangrene.* Although infections with toxin-producing, sporulating anaerobes occur largely in war times, cases appear from time to time in general and especially surgical practice. These infections are caused by members of the genus Clostridium, such as Cl. welchii, oedematiens, oedematis-maligni and others, which are characterized by their ability to produce powerful toxins. It has proved practicable to manufacture antitoxins against these toxins, and such preparations are indicated in all infections of this type and should be injected intramuscularly. Like other antitoxins their efficacy depends upon their early administration. Being antitoxins the protection they give is transient, but along with appropriate surgical treatment of the infected wound they are frequently successful in the treatment of these otherwise intractable and often fatal infections.

8. *Influenza.* This disease still baffles the bacteriologist and immunologist even more than it does the physician. While the Pfeiffer bacillus and the Dialister pneumosintes are variously believed to play an etiologic rôle, it can be stated that the case for neither has been definitely proved. This being so, it has been impossible to develop any specific biologic agent either for the prevention or the treatment of influenza. Bacterial vaccines, containing the Pfeiffer bacillus either alone or in combination with other bacteria associated with respiratory infections have been tried and are still extensively used. Influenza being primarily an intoxication, it is not reasonable to suppose that injections of killed bacteria would produce any antitoxic immunity and they undoubtedly do not. There seems to be little scientific warrant for including the Pfeiffer bacillus in such vaccines. Such other organisms as are included in these "influenza" vaccines may possibly raise the level of immunity to secondary invaders and thereby reduce the incidence and severity of these secondary infections, but the same comments as made on vaccines for colds apply equally here.

9. *Measles.* Until about eleven years ago measles had never been subjected to the study that its importance called for. A new era of investigation began, however, at about the time of the announcement in 1917 by Tunnicliff that she had succeeded in isolating a green, anaerobic diplococcus from the blood of measles patients. A year later Nicolle and Conseil in France and Richardson and Connor in this country reported the successful use of convalescent serum in children exposed to measles. Tunnicliff's later researches have borne out and amplified her original findings and these have been confirmed by Cary and Day, and Duval and Hibbard, and

a somewhat similar if not identical organism has been isolated from measles patients by Ferry and Fisher. These reports have stimulated renewed study of measles and the results of these studies to date may be summarized as follows:

A green producing diplococcus or streptococcus has been isolated from the blood and throat of patients in the early stages of the disease. This organism yields an extracellular toxic substance which, used in a manner similar to that of the Schick and Dick tests, produces skin reactions in the majority of persons who have never had the disease. This toxic or reacting substance is neutralized by measles convalescent serum. The serum of goats immunized with this organism not only neutralizes this toxin but, as reported by Hoyne and Gasul, Hoyne, and Halpern, prevents or modifies the disease in persons exposed to infection. A similar serum has been obtained from a horse by Tunnicliff and White, but it is still too early to pass any opinion upon its value.

Degkwitz has claimed that measles is caused by a filterable virus often associated with a green producing coccus, and has obtained a serum from sheep immunized with these organisms. The reports on the use of his serum are contradictory. So far, therefore, it must be remembered that all these claims are still on experimental trial.

Convalescent serum, however, may be accepted as a valuable agent in preventing measles, or better for modifying an attack so that the patient while being spared any harmful effects of the disease is permitted to develop an active and presumably lasting immunity.

There are difficulties in obtaining an adequate supply of this convalescent serum, but the difficulties are not insuperable unless large numbers of exposed persons are to be treated. The blood should be taken only from individuals who are definitely known to have had measles and then as *soon after convalescence* as possible. Should such a source of supply be lacking the blood of persons with a history of previous measles may be used. The usual strict precautions to be observed in the case of all human serums, such as the donor's freedom from communicable disease, and the sterility of the serum, should be observed.

Richardson and Jordan advise a dose of from 6 to 10 cubic centimeters, given intramuscularly. When injected within the first four or five days after exposure (counting two days additional from the date of the appearance of measles in the person to whom the contacts were exposed) the disease is usually prevented. When given later this dose generally prevents a severe attack but may allow a mild form of the disease to develop, which establishes a lasting active immunity. The dosage cannot be accurately determined because serums vary in their protective power. The age and size of the person receiving the serum also influence the amount to be injected. In general, it may be said, that at the present time convalescent serum is a valuable agent for protecting young and susceptible children against a malady, which without the serum may cause harmful and sometimes fatal results.

10. *Meningitis.* In epidemic cerebro-spinal or meningococcus meningitis the use of antimeningococcic serum has brought about a marked reduction in fatality and in the physical damage that follows such infections. Its administration is indicated in every case of meningitis due to meningococcus and may be given to advantage in many cases before a definite bacteriologic diagnosis has been established. All such serum produced in laboratories under the supervision of the United States Hygienic Laboratory is polyvalent, and contains antibodies for strains of the various agglutination and tropin groups. It should always be administered subdurally and at the earliest possible moment. When injected into the spinal canal the dose should be slightly smaller in amount than the spinal fluid withdrawn, and it should be injected slowly and under gravity pressure—not by syringe.

The serum may also be injected into the ventricles, but this route is not commonly chosen except in severe or obstinate cases. Its injection into the cisterna magna is comparatively free from danger and is recommended by Ayer and others, particularly in child patients. The intravenous injection of the serum, advocated by Herrick and others, may be of benefit but theoretically at least, only in early stages of the disease. Directions for continued serum treatment can be found in text books and in circulars accompanying the product.

The practitioner should bear in mind that from year to year or where the infection is brought from other countries, the strain or strains of meningococcus causing the infection may be of a type not covered by the usual serums. In every case of meningococcus meningitis, wherever possible, the organism present in the spinal fluid should be isolated and carried under cultivation. Then, should the patient fail to respond satisfactorily to treatment with the particular preparation used, it may be possible by simple agglutination tests to select another lot or make of serum which will have a higher antibody content for the strain involved. Current reports indicate that more cases due to aberrant or atypical strains are occurring, and some of these strains are already being added to the other standard strains employed for the production of antimeningococcic serum. The serum treatment of meningococcus meningitis should, therefore, always be accompanied by careful bacteriologic and serologic control.

There is no specific serum for the treatment of meningitis due to other bacteria, unless we except those cases in which pneumococcus is concerned. Even here we should not expect any pronounced improvement to follow the exhibition of antipneumococcus serum, but the desperate character of such cases justifies the use of

this serum or of pneumococcus antibody solutions.

11. *Pneumonia.* Recent investigations by Goodner and by Barach show that the injection of killed pneumococci into the animal body is followed by a surprisingly rapid development of active immunity to pneumococcus of the type injected. Not only do animals so injected resist what would otherwise be fatal infections of live pneumococci but their serum protects experimental animals against injections of many times the number of pneumococci that would kill normal animals. The immunity produced appears to be strictly type specific. Goodner's experiments, however, show that this active immunity while developing a few days after injection of the dead pneumococci rapidly disappears and is practically absent at the end of two months. These facts, therefore, would cause us to believe that bacterial vaccines containing killed pneumococci might be expected to produce a quick active immunity against the particular type or types included in the vaccine but that the resistance to infection thus established would be of short duration.

The serum treatment of pneumonia is a subject concerning which contradictory views are held. Without going into a discussion of the many reports and opinions of clinical observers, it may suffice to say (and the statement will likely be challenged) that antipneumococcic serum of Type I and of a potency equal to the government standard, given in sufficient dosage early in the disease often favorably influences the infection. We know that in pneumonia patients receiving intravenous injections of this serum, there is a temporary and sometimes permanent sterilization of the blood when a bacteriemia exists, there is often a sharp change for the better in the general condition and recovery may take place with accelerated crisis. Theoretical considerations would indicate that such serum would have no favorable and possibly a harmful effect if the infection is massive or of more than three or four days duration; and this prediction is borne out in practice.

Students of anti-pneumococcus immunity know that while it is possible to produce an immune serum containing agglutinins and protective antibodies, particularly against Type I pneumococcus and to a lesser degree against Type II, and while it is possible to transfer these immune substances to patients suffering with lobar pneumonia, such serum has distinct limitations because of its relatively low content of antibodies. Huntoon sought to concentrate the protective substance by absorbing it from the immune serum with pneumococci, then dissociating it. By this means he was able to free the antibody from other serum proteins, but this purified and concentrated antibody gave disappointing results in treatment. Felton has accomplished a similar concentration but by a chemical process. The Felton pneumococcus antibody solution contains protective substances against the first three types of pneumococcus, nearly free from accompanying serum proteins. According to Cecil, Rosenblüth, Bullowa and others this preparation given intravenously early in the disease lessens the fatality, especially in patients having a bacteriemia. Its action appears to be most favorable in Type I infections, somewhat less so in those due to Type II, and least favorable if not actually harmful in infections due to Type III organisms. Briefly then the Felton antibody solution is worthy of trial in cases of lobar pneumonia due to Type I and II infections if it can be administered early in the course of the disease.

In bronchopneumonia, a course of injections of mixed "cold" or "influenza" vaccines may, if the claims of some clinicians be true, ward off or lessen an attack. For several reasons it is difficult to see why this is so, but the meagre possibilities already discussed in this connection may apply in such cases. The distressing features of such infections and their seriousness lead one to employ any harmless agent that offers any promise of giving protection, and so the use of vaccines has some justification.

Unfortunately we have no serums that influence the course of the bronchopneumonias, once they are established.

12. *Puerperal Fever.* The hemolytic streptococci have recently come in for renewed attention. Immunological studies seem to indicate that streptococci causing the infections of the puerperium constitute a group by themselves. These cocci, like the related erysipelas and scarlatinal streptococci, produce a toxin-like substance against which an antitoxin has been prepared. Being an antitoxin this serum might be expected to alleviate the toxic symtoms and probably does, but in puerperal fever the septic processes are of greater consequence than the purely toxic process, and hence we should not expect this agent to have the curative value that scarlet fever antitoxin has in scarlet fever.

13. *Rabies.* This disease presents a problem of increasing seriousness in this State. The two questions that are pertinent to this discussion are, can dogs be protected by vaccination?, and which form of vaccine treatment should be given to persons bitten by or otherwise possibly infected by contact with rabid dogs?

A careful reading of some of the publications describing the experimental immunization of dogs by vaccinating them with a vaccine of killed rabies virus convinces one that the results do not fully justify the conclusions. There is one reliable report to the effect that dogs so vaccinated are not always resistant to infection with some strains of street virus, and there is little evidence as yet as to how long such immunity as may be produced actually persists. From what we know of these viruses and their immunizing action, we should not expect that a single injection of such a killed virus would produce a high

degree of immunity or an immunity of long duration. While it is possible that this method of vaccination may protect many dogs for a shorter or longer time from infection from the bite of some rabid animals, it by no means saves some canines. Authentic reports are at hand that dogs receiving not only one but two doses of such vaccine have developed rabies following the bite of a rabid animal some months after receiving the treatment.

In the case of human beings bitten by or suffering less violent contact with rabid animals, treatment with rabies vaccine will practically always prevent the disease. The vaccines offered are the original Pasteur vaccine, containing live but attenuated rabies virus, that of Högyes, a diluted suspension of attenuated fresh virus, the one recommended by Harris which contains the live virus in desiccated condition, the dialyzed vaccine of Cumming and the killed virus vaccine of Semple. All these preparations, when administered according to the prescribed schedule usually prevent the development of the disease. Rosenau writes that "it is not possible to state which of the various methods gives the best protection with the fewest complications." Because of the fact that vaccines containing living virus may in some few instances cause paralysis, there is a growing tendency to employ those preparations which contain killed virus, like that made by the Semple method. The fourteen day treatment is usually sufficient where infection from contact is feared or where the bite was trifling, but in other cases the treatment can with greater safety be increased to twenty-one days.

14. *Rheumatic Fever.* Although some late publications, notably those of Small and of Birkhaug, give the idea that the riddle of rheumatic fever is solved, the solution is neither so simple or sure. Here it is claimed that a particular coccus is the cause of the disease and its train of distressing and obstinate symptoms. A toxin is said to have been produced which, used in intradermic tests, denotes susceptibility or immunity to the disease, but the evidence is neither clear nor convincing. Here, too, an immune serum has been obtained about which widely diverging reports are heard. It is by no means certain that "Streptococcus cardioarthritidis" is the cause of rheumatic fever, and we must await the results of further investigation before passing judgment on the biologic agents now available.

15. *Scarlet Fever.* The recent development of biologic means for the prevention and treatment of scarlet fever deserves a lengthier discussion than can be granted here. It now appears to be established that hemolytic streptococci of a special biologic group are responsible for the various morbid manifestations classed as scarlet fever. These cocci, under suitable cultural conditions, yield a soluble substance which produces a local reaction when injected into the skin of persons with a negative history, and no reaction in the skin of those giving a positive history of scarlatinal infection. This same toxic substance in large doses produces all but the septic symptoms of scarlet fever and in smaller, properly gauged amounts produces immunity to this disease. Both these streptococci and their metabolic products can be used to immunize horses, and their serum, used either directly or in concentrated form appears to be a valuable remedy for this disease. The use of this toxin in the Dick test gives in the main a trustworthy indication of susceptibility or immunity, but in individual cases there occur reactions, usually false negatives, which do not correctly indicate the true immune status of the individual. Simultaneous tests performed on a considerable number of persons with toxins from different strains of scarlatinal streptococci, give like results in the majority of persons, but sometimes individuals show a definitely positive reaction to one toxin and a negative reaction to a toxin of another strain. This finding would explain the occurrence of negative reactions to the Dick tests in patients in the early stages of scarlet fever, and the development of typical scarlet fever in persons previously giving a negative reaction to the test. The accuracy of the test would probably be increased by using a preparation of the combined toxins of several authentic strains of scarlatinal streptococci, and it is quite likely that by increasing the amount injected into the skin from one to two skin test doses the occurrence of false negatives would be prevented.

The use of this toxin for actively immunizing susceptible persons against scarlet fever is likewise generally successful but here again persons so treated and giving a negative Dick test have come down with a characteristic attack of the disease. The comment made in regard to the Dick test applies equally in this connection, and a polyvalent toxin would seem to be a better means for bringing about an immune condition. The present practice of giving a series of five injections of toxin with the preliminary and subsequent Dick tests, while evidently resulting in a higher percentage of immunes is time consuming, and expensive from the patients' standpoint.

In some susceptible persons the initial immunizing dose of toxin may cause a systemic scarlatinoid reaction, the severity depending upon the dosage. In order to obviate such reactions a toxin modified by sodium ricinoleate has been devised and advocated by Larson. One dose containing roughly 3000 skin test doses of toxin is given, and systemic reactions are unusual. Reports of the efficacy of this agent are not in agreement, and cases are known where two injections one week apart have failed to protect against the disease.

Scarlet fever streptococcus antitoxin is now an accepted remedy for scarlet fever. Given a potent preparation, administered in sufficient amount early in the disease and the curative effect is gratifying not only in its rapidity but in its completeness. Chemical studies have re-

sulted in a refinement of the product and in a more reliable and conservative estimate of its potency. Volume for volume well aged batches of the concentrated antitoxin now cause little if any more serum sickness than concentrated diphtheria antitoxin. Being an antitoxic and not an antibacterial serum, its action is against the intoxication of the disease and not the septic complications. Inasmuch as septic sequelae are more likely to develop in a body depressed by a toxemia, one would expect that the complications of this disease would be fewer where the antitoxin is administered early. The expectation is fulfilled in practice. The antitoxin, for the best results, should therefore be given as soon as the diagnosis can be made. The dose is from ten to fifteen cubic centimeters of the present standard preparations for mild cases or cases of moderate severity in children with twice or three times the amount in older persons or in more grave cases. The injections should be made intramuscularly, and in the more virulent cases some of the antitoxin may be given intravenously.

The prophylactic use of this antitoxin, except under certain circumstances is not advisable. The number of exposed persons who eventually develop the disease is small, the protection afforded by the serum is brief, while the source of infection may continue to be present or new sources occur, resulting in infections after the passive immunity has worn off. Subsequent injections of antitoxin are then far more likely to cause a severe attack of serum sickness.

Where those persons who have suffered exposure to scarlatinal infection can not be seen regularly or frequently it may be desirable to give a prophylactic injection of five or more cubic centimeters of the antitoxin, but in all other instances it is better to examine contacts daily and at the first symptoms suggestive of scarlet fever to give a therapeutic dose of the antitoxin. In this way unnecessary sensitization to horse serum is avoided and any attack of the fever can be stopped before it has a chance to develop.

16. *Smallpox.* The smallpox vaccine virus of today is a standardized and refined product. It contains the living virus of vaccinia or cowpox free from all harmful bacteria. It may include a negligible number of harmless saprophytic organisms. The vaccine, containing as it does the living vaccinia virus should be given more careful handling than it frequently receives. Only fresh lots should be used and these should be kept continuously in an ice-cold place. In order to obtain the best results, strict attention should be paid to the method of vaccination which is described in the leaflet accompanying each package of the vaccine distributed by the Massachusetts Department of Public Health, and which has also been published by Leake and by White.

The older methods of cross-hatching, incision and linear scarification should be abandoned, and the simple painless and wholly satisfactory technic of multiple pressure be used instead. The method of single or multiple puncture is not to be recommended because recent reports show that undesirable results may follow. Vaccination by intradermic injection, as lately advised by Toomey and Hauver holds dangerous possibilities and should not be used.

When vaccinations are performed by the multiple pressure (Kinyoun) method, no dressings should be applied to the vaccinated site and under no circumstances should shields or tight bandages be applied. Shields are an abomination and their manufacture should cease. Vaccination should always be performed on the arm and never on the leg. If any untoward reaction occurs, if the vesicle or pustule is injured or broken, or if the scab comes off prematurely, the vaccination wound may be painted with tincture of iodine or a 4 per cent. alcoholic solution of picric acid, which if applied more than 48 hours after vaccination will not interfere with the development of immunity. Then such care as is indicated should be promptly given.

Too great stress cannot be given to the importance of vaccination technic. Fresh virus, applied by the multiple pressure method, will give a maximum of "takes" in first vaccinations, a maximum of accelerated "takes" or immune reactions in revaccinations, with a minimum of discomfort and undesired results.

Careful attention, especially in revaccinations, should be given to the appearance of vaccinoid or accelerated "takes," and of immune reactions. The vaccination site should, therefore, be observed on the third day and twice later, usually four and eight days after vaccination. The various reactions following vaccination have been excellently described by Hooker and also by Leake.

The ideal plan for vaccination is to vaccinate babies during their first year of life and again just before entering school. During epidemics and where definite exposure is known to have taken place revaccinations should be performed.

Smallpox vaccines, other than the present dermo-vaccine obtained from calves have been put forward with claims of superiority. The testicular vaccine of Noguchi, the neuro-vaccine of Levaditi and various vaccines treated with a variety of chemical agents have been tried and some of them are in use in different parts of the world. They appear to possess no distinct advantages over the calf vaccine and at present are not to be recommended.

17. *Tetanus.* Although tetanus infections are fortunately few in this State, their possibility must always be considered in wounds due to firearms, fireworks or with wounds on dirty surfaces or into which dirt enters. Here, tetanus antitoxin, promptly administered usually averts the development of the disease. This, like other antitoxins, is now available in more refined and concentrated form. The prophylactic dose is usual-

ly 1500 units which should be given immediately after the injury occurs and repeated each time there is to be surgical interference with the wound. In treatment the antitoxin should be given intraspinally at the first possible moment and frequently thereafter, using as large doses as can be conveniently injected. The antitoxin should be diluted if necessary. Additional amounts may be given intravenously and in the nerve sheaths, although experimental studies show that the intraspinal injection is by far the most efficacious.

With the development of diphtheria toxoid a toxoid made from tetanus toxin has been announced by Ramon. This preparation induces active immunity to tetanus and should be useful in protecting troops in wartime, and in protecting susceptible domestic animals. Its use after a wound or infection is received would of course be futile.

18. *Tuberculosis.* In tuberculosis we have the several tuberculins for diagnosis and treatment, and now much attention centers about the new prophylactic vaccine of Calmette—"B. C. G." The tuberculin of choice for diagnosis is the "Old Tuberculin" or "O. T." This product is standardized for method of manufacture and sterility but not for potency. This is unfortunate because the physician may not know what the strength of a preparation is, or, as a matter of fact, if it has any strength at all. Before using "O. T." inquiry should be made if the product has been tested and what its strength is as compared to preparations of known activity. For treatment, the "Old Tuberculin," the "Bouillon Filtrate," ("B. F.") of Denys and the "Bacillus Emulsion" or "B. E." comprise all the necessary tuberculins. Ophthalmologists show a preference for "T. R." but it probably has no superiority over "B. E." for their purpose. One should always bear in mind that tuberculin may be a dangerous agent and no liberties should be taken with the prescribed dosage, save by those who are thoroughly familiar with its action.

Calmette, Guerin and others have announced that in "B. C. G." they possess a vaccine that is harmless, yet when given to young non-tuberculous animals and children causes an active immunity to be established against tuberculous infection. This vaccine is composed of tubercle bacilli made avirulent by successive culture in a bile-containing medium. It is given by mouth to infants in the first few days of life. Sometimes the vaccine is administered subcutaneously. The history of the infants and animals so far treated and later exposed to tuberculous infection is at first reading impressive—so impressive that extensive experiments on children and bovine creatures are being carried out in this and foreign countries. Any final judgment, however, must be withheld until these tests have been multiplied and continued over a period of years.

For the cure of tuberculous affections the "Sanocrysin" treatment has come out of Denmark where among some observers it has found favor. The treatment consists of the injection of a gold salt along with an anti-tuberculous serum. The treatment has been investigated at the United States Hygienic Laboratory and the results have discouraged its use. It can be safely said that outside of the tuberculins we have no specific biologic agent of value in the treatment of infections due to the tubercle bacillus.

19. *Typhoid Fever.* There is little new to be said about typhoid vaccine, and as yet there is no specific serum or other biologic agent for therapy. Since the two types of paratyphoid infections have become prevalent in this country, it is customary to include bacilli of the A and B types in the so-called "triple vaccine" containing also typhoid bacilli. Since 1921 all the vaccine of this kind that has been distributed by the Massachusetts Department of Public Health has been made according to the numerical standard current in the United States Army and Navy and in commercial laboratories. In addition, since 1924, the bacilli have been washed. This step has reduced the number of systemic reactions without diminishing the immunizing effect. In immunizing adults it appears to be the better practice to inject this vaccine in divided doses, giving 0.2 then 0.5 c.c. followed by two injections of 1 and 1 c.c. all at weekly intervals.

Besredka, believing that we should immunize the particular tissue vulnerable to typhoid or paratyphoid infection, has, after much experimental work, proposed giving typhoid vaccine by mouth. A preliminary dose of bile is administered for the purpose of exposing the tissue cells of the intestinal mucosa, particularly those of Peyer's patches, to the action of the vaccine. He has practised the method on groups of French troops and civilians, and although his figures seem significant so far as freedom from typhoid infections are concerned, his method is little used in this country.

The injection of typhoid and other vaccines as well as milk and various proteins in the treatment of typhoid and allied fevers still remains in the realm of empiricism, and further information must come from clinical studies.

20. *Whooping Cough.* The value of bacterial vaccines for the prevention and treatment of whooping cough is a moot question. They are of two kinds, namely, the simple vaccine containing only the Bordet-Gengou bacillus and the combined, made from this bacillus and other bacteria commonly isolated from the respiratory tract. From a critical standpoint it may be objected that this bacillus has never been positively proven to be the cause of whooping cough, and at best it has relatively poor antigenic properties. One, therefore, should not expect any marked degree of protection to result from injections of vaccine made from it. The value of the other organisms included in the mixed vaccine is sub-

ject to the same criticisms that have been stated elsewhere in this discussion. Clinical reports as to the ability of vaccine treatment to prevent or mitigate an attack of this disease are not in agreement. The majority of these reports are uncontrolled and, therefore, the worth of their evidence should be discounted. The Danish reports are favorable as is also the report of the Harvard Whooping Cough Commission. A critical analysis of the latter report, however, shows an absence of proper controls, and that the results obtained with the vaccine were not clear cut or convincing. In other series of observations extending over a period of several years where children were vaccinated with small and large doses of fresh and old vaccine and where alternate unvaccinated children were used as controls there was no appreciable difference in the whooping cough experience between the vaccinated and unvaccinated children.

While there are many enthusiastic users of pertussis vaccines, the whole evidence would seem to indicate that such vaccines, whether simple or combined, are of doubtful value, and rank low in the list of biologic agents.

21. *Non-specific Protein Therapy.* The use of proteins, introduced into the body by parenteral routes, for the treatment of various infections offers a wide and little studied field for investigation. There is probably no subject in immunology that is so difficult of scientific approach as this non-specific therapy, and such information as we have has been gleaned by the clinician. The injection of typhoid or coli vaccines, and of such protein substances as milk and peptone into patients suffering from typhoid and other enteric fevers is said to be followed by improvement in the condition of the patient. Horse serum, beef serum, antitoxin, in fact a whole array of proteins have been employed in treating many acute and chronic infections and truly remarkable effects have been claimed for them. The nature of their action is unknown, and can only be guessed at, and the only information that we have has come from the observation of subjective and objective symptoms following their administration. Until we have some clues as to the physiologic processes involved by their injections no critical analysis of their value is warranted.

The list of serums, vaccines and other biologic products now offered to the physician is long; the number of infections, acute and chronic, tempting one to find a means for prevention, alleviation or cure is large. For some of these infections we have specific biologic agents that stand on a sound scientific basis, there are others with some slight theoretical and some clinical evidence to sanction their use and there are still other preparations that are offered and used with little or no justification. As time goes on, more and more preparations will appear, and they should always be subjected to the closest experimental and clinical scrutiny before they are accepted. The prevention and treatment of infectious diseases by biologic agents rests on solid ground, and its future depends upon the critical thought and conservatism of its disciples.

CHAIRMAN BLACKFAN: This timely and very complete resume of the situation from Dr. White's point of view concerning the use of these so-called biologic products will be discussed first by Dr. Denny of Brookline.

### DISCUSSION

DR. FRANCIS P. DENNY: *Mr. Chairman and Members of the Section:* In regard to vaccination against smallpox and the use of toxin-antitoxin against diphtheria the great need, I think, is to get these two measures employed early in life. We do not appreciate how much exposed a baby is, for example, to smallpox when there are cases about. The first case of smallpox I ever saw, about 1900, was in a baby in Brookline, with no history of exposure whatsoever. This child came down right out of a clear sky.

We are apt to let the best time for the first vaccination slip by, and that is the time when the baby is being nursed, early in the first six months. There is less reaction at that time. The baby apparently carries over some of its mother's immunity and then the breast milk is a great protection against severe reactions.

I would like to speak of measles convalescent serum. It is certainly very wonderful in its effects. Such a small amount as six c.c., a teaspoonful and a half of serum, will either prevent the disease, or what is much better, transform a severe, serious, dangerous disease into one that is exceedingly mild. I think we ought to use more of this convalescent serum until such time as we have a serum produced from animals.

In regard to toxin-antitoxin, I thought the best contribution to this discussion I could make would be to show this chart which gives the results of the use of toxin-antitoxin in Brookline. This solid line represents all the cases that have occurred since 1905. This dotted line represents children under fifteen years. This red line represents the deaths.

We were rather slow in starting this work in Brookline. I regret to say I was very skeptical at first about its benefits. In 1922, we had an unusually large amount of diphtheria. That stirred us up, so that in 1923 we got the money for the work and went at it very energetically. We got about 2600 children in the public and parochial schools tested and given the toxin-antitoxin. To date we have records of 5600 children that have been protected. We have no record whatever of the cases that have been protected by physicians in their private practice, but we have reason to believe that a good many have been protected in that way. I think it is safe to say that three-quarters of the children under fifteen years of age have been protected.

The result is shown here. In 1923, the year we started, we were still suffering from the epidemic of the year before and most of the cases occurred during the first six months before we really got started. We had about forty cases and one death. The next year, however, (1924) the cases had dropped to 16, with no deaths. That was the lowest we had ever had. The next year, 1925, 10 cases; 1926, 8; and 1927, 9. Thus far this year we have had 3 cases reported, one of which is just a bacteriologic case.

How much of this decrease is due to the toxin-antitoxin? There have been marked variations in the disease in the past and there is a feeling that the last three or four years have been off years for diphtheria.

Of special interest in that connection is the ages of the cases that we have had. I show you here the number of cases under five years. The difference between the dotted line and the dark line represents those over fifteen. In 1925, the adults are roughly very much as they often had been, but the children had dropped to three. In 1926, there was but one child, and that was a fourteen year old boy. In 1927, there were only three. Taking the four-year period before 1923, children under fifteen represented 82 per cent. of the cases. In the four years following 1923, the percentage of children was 38.

I think it is perfectly evident that the children are being protected against diphtheria by toxin-antitoxin. (Applause.)

The Chairman then introduced Dr. Richard M. Smith.

Dr. Richard M. Smith (Boston): *Mr. Chairman*, there is very little that one can add to the paper which Dr. White has given. The most one can hope to do is to emphasize perhaps some of the facts which he has brought out and to record personal experiences in the use of the various products.

He has discussed the use of these products in relation to three different situations with which we are confronted. First, the treatment of individuals who are ill with disease; second, the protection of those who have been exposed to disease, and third, the protection of individuals who have not been exposed, that is, the production of immunity on the theory that later they may be exposed.

With reference to the treatment of individuals ill with disease, there are two or three comments I should like to make. First, with reference to poliomyelitis convalescent serum. The fact that we can now tell parents that there is a method of treatment which offers a reasonable chance of being effective is a tremendous boon. All of us have been distressed at a situation when in the presence of exposure to or of infection with this disease all we have been able to say was, "There is nothing we can do." Now we are in a position where we can offer some hope for the prevention of paralysis if the diagnosis is made early.

With reference to erysipelas, it is important to bear in mind that infants under two years of age have a very high mortality, perhaps fifty per cent. We have had some experience at the Infants' Hospital in Boston in the use of erysipelas serum, and of the last 19 infants under two years of age, we were able to give 16 of them the serum within the first three days of the disease, and all of these children lived. The other three infants were admitted after the disease had been in progress more than three days, and they all died. In this connection we ought to remember what Dr. White said, that if we are unable to get erysipelas serum, scarlet fever serum is effective and should certainly be used.

With reference to meningococcus meningitis, I simply want to emphasize a point which Dr. White brought out, that we must test in each instance the efficacy of the serum used for the individual patient. We have over and over again found that children admitted to the hospital ill with meningococcus meningitis, were infected with a particular strain of the organism which was not influenced by the serum which we ordinarily used. We have had to secure other serum, and when an effective serum was found cure has been produced, but we have had certain cases for which we were unable to find any serum that was effective. As you are aware, meningococcus meningitis in infants is very frequently followed by sequelae, the most common of which is hydrocephalus, which are unfavorable, even though the life of the individual may be spared. As a routine procedure in all infants we give the serum intraventricularly as well as intraspinally on alternate treatments for the first few days, and by this method we have greatly reduced the incidence of these unfavorable sequelae.

I should like to raise a question for Dr. White to answer, whether or not he would recommend the employment of scarlet fever serum in all individuals ill with the disease or whether or not in individuals who have a very mild infection it is necessary to use it. We know, of course, that the serum is primarily effective against the toxin of the disease, and that it influences the complications only to a slight degree.

We have had some experience at the children's hospital in the use of Small's antitoxic serum in the rheumatic infections. So far as our experience goes, it has been entirely unsuccessful. We have not been able to influence the course of the disease or to improve the condition of the patient. There have been a few individuals with chorea who have improved following the use of the serum. But they had been ill so long before the serum was given that they were at a period of the disease where they ought to have improved in any event, so we can't give the serum the credit for improvement.

So far as the treatment of individuals who are exposed to disease is concerned, there are three or four conditions with which we are concerned

—first, measles. I think that I have nothing to add to what Dr. White and Dr. Denny have said except to emphasize the value of the use of convalescent serum. It certainly is a great satisfaction to have something which we can use in selected cases, either in very young children or in children whom it is particularly important to protect from the disease, I believe it is better in most instances to give it after the first four days in order that the children may have a mild form of the disease and obtain immunity than to give it early and simply protect them from that attack but leave them susceptible to subsequent infection.

I should like also to emphasize the importance of protecting children who have been exposed to rabies by the use of material which is now available. It used to be a very long and painful process to give twenty-one injections, and then we were dealing with a virulent virus. It was a source of some anxiety lest we might produce paralysis. But now that we have a perfectly safe material and the number of injections have been reduced to fourteen, it seems to me there is no excuse for ever allowing exposed individuals to go untreated.

There is a question frequently raised with reference to the procedure to be followed in a family where one child has scarlet fever, whether it is advisable to do Dick tests, and if the other children are susceptible to scarlet fever, that is, if they have a positive test, to give them protection by the use of scarlet fever serum. Personally I think that it is not advisable to do so in usual instances, because in the first place the incidence of secondary infections is very small and secondly we have a means of treatment at hand which can be given early provided infection should occur, and thirdly reactions from the use of serum still occur, although they are not so severe as formerly.

With reference to the protection of unexposed individuals, that is the actual routine procedure, if you choose to call it so, for protection against disease. There are three conditions which it is important for us to bear in mind. First, smallpox, about which it is necessary to say nothing except that we are frequently very derelict in the giving of vaccination because we are accustomed to believe that the chances of exposure are so small. We still hear the statement, "There isn't any smallpox; why should we vaccinate?" Second, diphtheria I believe toxin-antitoxin should be as universally employed as smallpox vaccine, although that custom is not yet universally in vogue. My personal experience would indicate that we can secure a very high percentage of immune reactions after the use of the toxin-antitoxin which is furnished by the state.

Third, typhoid fever. My own feeling is that this is a disease that is a disgrace for any doctor to have in his practice, provided he has had the family under his care previously, because it is a disease which need never occur, or practically never occur if repeated inoculations are given. I believe that we should be just as active in our immunization against typhoid as we are against smallpox and diphtheria.

There is only one other condition that I want to mention and that is whooping-cough. As Dr. White said, there probably is no subject about which there is so much difference of opinion. It is very difficult to approach the subject from an entirely impersonal point of view, and to separate one's impressions from the actual facts which can be proved from controlled experiments. However, it does seem to me that one's impressions over a considerable period of time are worth some consideration, and I have a strong feeling that if we use the right kind of vaccine in the right dosage, it is of some value in protecting against the disease, and if given early, also tends to modify the severity of the infection. (Applause.)

The Chairman then introduced Dr. Stansfield of Worcester.

DR. OLIVER H. STANSFIELD: These remarks will necessarily be somewhat disjointed and the basis must be personal experience. I would like to say something in the first place about the sensitization to serum in general. Back in 1915 at the Municipal Hospital in Philadelphia I tested out a hundred successive admissions to the diphtheria side with one-tenth of one c.c. of 1 to 10 horse serum, and per hundred patients, 84 reacted. They were all given an ordinary curative dose of antitoxin, nevertheless, and we had no reactions. Ever since that time I have been thoroughly skeptical about the production of any anaphylactic state by therapeutic injection. I would not give serum to a bronchial asthmatic, however, without due care.

Those results were not published for the simple reason that they were so opposed to generally accepted ideas that we didn't dare. Within the last month I have seen a report that bore out the thing absolutely.

With erysipelas serum my results have been very satisfactory. Perhaps I have been lucky. I have seen four cases in the last few months, and none of them was over twenty-four hours old. They have all done very well. I rather think from the way the patients behaved that the serum is antitoxic and not bactericidal. The disease slowly goes on for perhaps forty-eight hours, and one continued to seventy-two hours, but the temperature comes down and it terminates in about seventy-two hours.

I can't say anything about the influenza vaccines. In June, 1918, we had in one day a series of over a hundred admissions of soldiers, and they all took identically the same course. They had a sudden onset of fever of 102 or 103, or perhaps a little higher, that continued for three or four days, then dropped to a normal temperature within twenty-four to thirty-six hours, and then a secondary rise. It is on the secondary

rise that all the complication begins. I rather feel influenza is probably that first three or four days' fever with the secondary rise, and in those who had no complications, the secondary fever dropped to normal within twenty-four hours and the patients got perfectly well. I wonder if it would not be a good idea to investigate that first fever attack. This winter I have seen some half dozen identical cases, some that got well after the fever dropped the second time and some that continued on with pneumonia, the very bloody type that we get in influenza.

As far as meningitis monovalent serum is concerned, I think it is very dangerous. You can refer back to the British experience in 1914 and '15. With the appearance of the Canadian troops in England, they began to get a lot of meningitis for which the serum on that side was no good, and it was only when they got the organism produced from that epidemic that they began to get curative value. So in making meningococcus serum, I think we have to take all four types and mix them up.

As far as smallpox vaccine is concerned, I do not think Dr. White need be duly exercised about the impurities. I think most of the trouble found in smallpox vaccines is due to carelessness after the thing has been done. With scarlet fever serum my own feeling is that it is as much needed as in diphtheria. The disease is cut off in about twenty-four hours at the most, so far as I can see. My own preference as to serum there is Dochez's serum, largely on the grounds that it is more likely to be a bactericidal serum, as well as an antitoxic serum, than the Dick. If that is the case, the aseptic complications that may follow may be probably cut down.

I would like to ask Dr. White especially if he thinks that the injection for immunizing dogs against rabies is worth while.

As far as whooping-cough vaccine is concerned, it is very doubtful. Just the other day a doctor friend of mine told me of his experience with four children. All four children have whooping-cough now. The two older ones were given vaccine and had severe cases. The two younger ones were not given vaccine and had it very mildly.

A few days ago in discussing a fatality in the case of streptococcic meningitis, (I didn't know then there was any community between scarlet fever serum and erysipelas serum) that perhaps we might be able to get results by injecting a mixture of scarlet fever serum and erysipelas serum into a case of a streptococcic meningitis.

The British method of immunizing typhoid fever is to use two injections, a half c.c., the same strength that we use. (Applause.)

Dr. Dwight O'Hara, Waltham: The use of convalescent serum in the prevention or modification of measles is effective and valuable. While the actual technic of administering it is simple, the practical technic is not so simple for those who are away from places where there is a supply of convalescent serum. One must get the serum before giving it, and then one is in duty bound to find a convalescent measles patient and bleed him in order to return the serum to the source from which he got it, which may be a considerable distance. I have, therefore, on several occasions followed the recommendation of injecting subcutaneously whole blood from the father or mother of the child, usually a 10 c.c. dose. In the few cases in which I have used this simple procedure, it seems to have produced the same result as convalescent serum in ameliorating the disease. It is almost as simple to do, and when it is done you do not have to hunt up a donor to pay back the borrowed serum. I would like to ask Dr. White if he would recommend this.

Dr. A. C. Eastman, Springfield: There are one or two questions that I should like to ask Dr. White. One is in connection with the blanching test of scarlet fever. How much dependence can be placed on that. I have had one or two experiences in questionable eruptions where I have tried it and apparently got nothing decisive. I would like to know whether it is due to the faulty toxin that Dr. White spoke of.

The other question is as to the relative value of autogenous vaccines versus stock vaccines. Most laboratory men tell us that stock vaccines are useless; that the only types that do any good are the autogenous vaccines. I have had one or two experiences where autogenous vaccines, carried out under laboratory direction, apparently had no effect at all, then trying a stock vaccine and apparently getting results.

The query arose in my own mind whether it is not possible that in certain chronic or subacute infections the individual organism may not lose a certain amount of its virility so that an autogenous vaccine made from that individual would not have any value, whereas a stock vaccine made from a virile organism might produce results. It is simply a query which has come to my mind as a possible solution for those rather unusual cases.

In connection with personal experience, as Dr. White said, it would seem that experience should count for something. In 1914, I started using vaccine as a routine treatment for whooping-cough, and not having any definite figures to give, my own impression is that I have gotten results as good from the vaccine as from any other method of treatment. In the majority of cases it seems that the number of attacks have been reduced and the period of time reduced. Also, in the small children and infants I have been in the habit of using a mixed vaccine. Dr. White spoke of the pneumococcus organism in mixed vaccines as being the one that perhaps did give results. I have used that in the hope that I would have fewer cases of bronchopneumonia developing in the infant, and I feel quite

positive that such is the result during these years.

Dr. Fred H. Allen, Holyoke: I should like to ask if any value is attached to the character of the pseudoreaction in the Schick test. Is the patient who shows a positive pseudoreaction more apt to give a reaction to toxin-antitoxin or is one governed entirely by the history of attacks of asthma or hay fever.

Dr. P. R. Withington, Milton: I have a series of cases in which I am very vitally interested. About Christmas time my baby had pneumonia. My three children were all exposed to measles. They were given convalescent serum with great efficiency, and none of them developed measles. Approximately three months later, the baby, who had not as far as we knew, been exposed to measles, came down with a very mild case. The other two children, five and six years of age, had slight colds at that time, but stretching my imagination to the utmost limit I could not say that they had measles. Since Christmas, two of the children have been in quarantine a total of seven times—one four times and one three times, with a sixteen-day quarantine each time, missing school consistently since then. The question is how long they have to go on being quarantined. Can I consider they have had measles?

Dr. E. P. Bagg, Holyoke: The function of immunizing nurses has fallen into my hands in the Holyoke Hospital. The thing that has impressed me in the last few years is the great number of them who are Schick positive. More than half of them are positive. In the last group that I did a week ago there were seven. Only one was Schick negative.

Dr. Roy J. Ward, Worcester: I should like to ask Dr. White if he would consider this experience an anaphylactic reaction: In June, I immunized a boy of about twelve years of age with three doses of toxin-antitoxin. In August, he stepped on a rusty nail and had a punctured wound. I gave him 1000 units of tetanus antitoxin at that time. I immediately went on my vacation. The story that I heard on my return home was that in three days he had a very virulent anaphylactic reaction which laid him up in the hospital for three or four days. The physicians who saw him at St. Vincent's Hospital did not know whether he really was going to have tetanus and had been immunized against it, or whether it was a virulent anaphylactic reaction.

I have heard reported that occasionally after the toxin-antitoxin had been given that there had been a history of some sudden death on the use of tetanus antitoxin. I should like to ask if that is true.

Dr. Warren R. Sisson, Boston: Since I have been in practice there have been two things that have impressed me. First, the poor records that the average private practitioner makes on clinical studies, and secondly the advantages that the private practitioner has in solving the problems which have been presented in such a discussion as this. I think that the opportunity such as has been reiterated by Dr. McKenzie of London in the past is almost unlimited, and it is the men in private practice who have the advantages of following in detail the efficacy of the various serological treatments.

I should make a plea for more concerted action and for the use of serums and vaccines which come from authentic laboratories. The criticism that one would have in regard to our personal experiences is that we use different doses, different vaccines, and our criteria of observation are so variable that our conclusions, when it comes to final analysis, have very limited value. With this in mind, this year I have attempted in a very small way to analyze about fifty cases which have come under my own personal observation in regard to the use of convalescent serum for measles. Nothing new I should say has come from my own personal experiences except again to make me absolutely convinced of the efficacy of this treatment and that it should be more widely used.

I should like to call attention to two points, one of which Dr. O'Hara has already mentioned. I have used (and it has been used, of course, many times) convalescent blood, whole blood, and there is no doubt but that this method of the administration of convalescent serum can be carried out successfully.

I should like to ask at this time if I understood Dr. Smith correctly in stating that one could obtain an abortive case by the use of convalescent serum when given after the fourth day after exposure. It is my experience that one cannot necessarily obtain any protection if the convalescent serum is given after the third or fourth day. I am sure this is true in some cases. Furthermore, it is impossible, with our present state of knowledge, to say whether we can abort or whether we can completely protect the individual. In many cases where small doses are given within the first four days, one can abort the disease, giving a very small dose. Very frequently it completely prevents the disease from developing.

In regard to the use of whooping-cough vaccine, here also I have attempted during the past year to take up the study of a series of cases, using the vaccine from the Harvard Medical School Commission, the vaccine being made under careful supervision. The records of the Danish workers are very convincing, and one would be loathe to discontinue the further trial of pertussis vaccine as a preventive and also as a treatment. I think it was more or less on the basis of that work that a new interest was taken by the Whooping-cough Commission at Harvard.

After using that vaccine in a series of about fifty or sixty cases, the conclusions still in my

mind are very indefinite. There seems to be little evidence that the administration of large doses of this particular vaccine has any effect whatsoever upon the disease if it is once established, if one uses control cases. The evidence that it may have some preventive effect if given a week or a few days after exposure is suggestive that it should be continued further.

DR. MAY SALONA HOLMES, Worcester: Dr. White has been asked about the use of the scarlet fever serum in mild cases, and I think I will just speak of our clinical experience. He has all my data, and I have talked with him. I do not know just what he will say today. For over twenty-five years we were treating scarlet fever without serum. It seemed to me that I could never see another case, I was so discouraged, but when the serum came in, we began to have different pictures and different results, and I get so enthusiastic about it now that I really hate to try to talk, I get so excited about it.

First, of course, the amount was limited, and we only used it for severe cases, and the results were very wonderful. We have cases in the hospital of children who have scarlet fever, although they had never had much fever, had never had very severe rash, were running along all right, but still never really got well during convalescence; they were having a nagging nasal discharge and a certain amount of adenitis which was varying from day to day in severity, so I thought we would try out serum in all cases. They had various little pustules around the fingers; also mastoids would develop in these mild cases most unexpectedly. My orders are now to my house doctors to give it to every case, and we have seen a great change. We do not get these sore fingers, and we do not get as much adenitis, and we do not get ears in those mild cases, so I think that it should always be used.

Then in the severe cases with complications, particularly late complications where patients come in late for treatment rather than during the first week of the disease, we give the serum, and we give just as large a dose as we would have given in the first place, and I think we do get results. Dr. White said he does not know why we get results but at the same time these are pus-reducing complications that come in scarlet fever. The streptococci, wherever they locate are pus-producing and there must be toxin circulating in those active complications. I think we want to stop it where it is. In the old days when these cases came along they would have suppurating glands anywhere; they would have abscesses in the abdominal wall; they would have septic arthritis, and go along for seven or eight weeks and then pass out. We don't see those cases any more because even if they start in with one of those difficulties, it stops at that point after we have given the serum. I think it has a great value.

I have a case in the hospital this week where I cannot see that anything helps but the serum. The man is in his third week of sickness. He had evidently had a very sharp attack of scarlet fever. He remained at home, because he thought he could stay there all right and he was getting up and going out during his second week, thinking he was all right. Then in the third week he began this very, very discouraging cellulitis of the neck, beginning around the glands of the right side, and then that indurating cellulitis started in and was circling the neck. The last night before he came into the hospital it traveled three inches from the median line on around the left side. Although his temperature was only 103, he was delirious. He received three bottles of Dr. White's serum. There was considerable acidosis, and his kidneys were not good, so he was given some glucose intravenously. He was given a good deal of shock treatment within an hour or so. He ran off into sharp anaphylactic reaction. He had a great deal done that morning, but I can't see that anything but the serum could have reached his real lesion. From that moment the temperature had dropped and he became very much better. The next day he was normal. The temperature has never arisen again, and the cellulitis has practically gone, now. He has had no systemic trouble. That is not the only case we have seen results in in late complications, so I do feel we always ought to give it.

DR. J. L. E. BRINDAMOUR, Holyoke: In relation to whooping-cough, I had an experience in 1925 that rather surprised me. I was at the time at St. Vincent's Hospital in Philadelphia, which had 350 children as patients. An epidemic of smallpox occurred in the vicinity of the hospital, and it was decided to use smallpox vaccine on all the children in the hospital. At the time, we had twenty-two children in the detention house who were ill with whooping-cough; they were whooping and coughing and were in pretty bad shape. Those children, as well as the others, were given the smallpox vaccine, and inside of two weeks everyone of them had stopped whooping. As a result of that, a chief of mine who had some patients in New Jersey decided to try it on four cases of whooping-cough there. I accompanied him, and we gave them the smallpox vaccine. Inside of twelve days those children stopped whooping. I tried it in my own practice in six cases, and I dare say that four of those six gave good results. If Dr. White has any suggestion on the matter I would like to hear it.

Along another line, we did in Holyoke, recently 2600 toxin-antitoxins. There wasn't enough money to go around to Schick these children, besides which the time for the immunity to develop had not yet elapsed. Two cases in particular came under my observation. A younger baby in the house had developed diphtheria and I was called in to see it. In order to further protect the older children who had gotten the toxin-antitoxin (the last injection had been given

about a week to ten days previously) I gave them the antitoxin and got two very beautiful reactions that lasted for about a week. They developed urticaria and it lasted for about a week, and we were not able to give them much relief with anything. I don't know whether I was justified in giving the antitoxin so soon after the injection of the toxin-antitoxin, but I thought it was the safer thing to do.

If Dr. White could answer that question I would appreciate it.

Dr. John Lovett Morse, Boston: If the last speaker will look back in the French literature of about thirty years ago, he will find a lot about the treatment of whooping-cough with smallpox vaccine. At that time I was young and enthusiastic and tried it out a little. As far as I could see, it did not do anything at all.

It has been very refreshing to hear such a sane and rational statement of what we really know about vaccines and sera as Dr. White has given. I wish I thought it would do any good. I feel quite sure, however, that while the general practitioner who reads his paper may be impressed at the time, he will forget all about it when he gets the literature from the various makers of these sera and vaccines and listens to the "spiels" of their salesmen. He has to keep up with the fashion, however, in order to keep his patients, because if he doesn't do all these things, some other fellow will, and they will leave him and go to the other fellow. Furthermore, it is only natural for a man to want to do something himself for his patients. Consequently he tries it, whether he thinks it will do any good or not. Unconsciously, moreover, physicians are a good deal influenced by their pocketbooks. They will not admit it, of course, and probably don't realize it. Nevertheless, they are. Therefore I don't feel Dr. White's paper is going to do much good.

I have been much impressed with the good results which I have seen from the erysipelas antitoxin in babies. I haven't seen as good results in children.

Just one or two words as to rabies. If you look in the dictionary you will find it has three syllables—ra-bi-es. In thinking of the treatment we must not forget that the treatment with nitric acid at the very start is almost as important as the treatment with the vaccine. This Semple vaccine is a great comfort, because you don't have to wonder every time you give it whether you are going to contract hydrophobia yourself. You don't see any results after the first four or five injections. After the seventh day, however, the belly is covered with swellings as big as hen's eggs. Every one looks as though it was going to form an abscess and burst. Luckily, nothing happens to any of them and they all gradually disappear.

With reference to the serum for rheumatism, I don't feel so awfully sure that we know what rheumatism is. Some of you have heard me say this before. I don't feel that we know so much about it as many think and, therefore, I don't feel certain or feel that it is even probable that an antitoxin is going to do any good.

Dr. Benjamin White then closed the discussion:

Mr. Chairman, I think we all owe Dr. Denny a vote of gratitude for making it possible for us to quote a Massachusetts town instead of a New York town in showing what can be done in the way of diphtheria prevention. It seems to me as though it is as thoroughgoing and complete prevention work as any with which I am acquainted.

I should like to add one point to what Dr. Denny said about smallpox vaccination in infants. In my remarks, in order to get them within the allotted time, I neglected to say that we are always advocating vaccination in the first year of age and again at school age.

Dr. Smith asked a question about giving scarlet fever antitoxin in all cases. All that I can say is I have to depend upon my clinical friends for their experience, and in putting out scarlet fever antitoxin for general use, it has seemed to us that we were on the safe side in advising it in all cases. Dr. Francis Blake, who has been testing a good deal of our serum for us, induced us to change our earlier opinion and to advise it in all cases. I should like to say also in this connection that there are undoubtedly some antibacterial substances in the serum. We make no claims as to their value but they are there, and, therefore, might have some effect in warding off complications.

I neglected to say anything about the prophylactic use of scarlet fever antitoxin. Dr. Smith took it up and I should like to emphasize his opinion about that. We are asked repeatedly whether this should be given in cases of contacts with scarlet fever. We have advised against it, for the reasons that he has stated, and an additional reason is that if you give scarlet fever antitoxin to a person who may have been exposed to scarlet fever, that person very likely may require it later, and then when you give the second dose, you may get an aggravated case of serum sickness.

Dr. Stansfield spoke about his preference for the Dochez scarlet fever antitoxin. The antitoxin put out by the state now is made by a combined method, but largely the Dochez method.

About rabies in dogs, I meant to speak about that because that is a question over which there has been a great deal of controversy. In going back in the literature recently I had access to Semple's original paper. After making twenty-eight successive daily injections in dogs, he found that some of the dogs were protected against rabies and some were not. If Semple's twenty-eight injections did not protect dogs, it seems to me ridiculous to expect that one dose of

killed virus would protect dogs for any length of time. If you will read carefully the literature of some of the Japanese, you will see that their conclusions are not justified and are altogether too enthusiastic.

Mohler, I believe it was, carried out some very careful experiments on dogs. He found some of the dogs injected with killed rabies vaccine were protected against some virus but not against all virus. We have no idea how long the protection lasts, and we have had reports of a number of instances where dogs had received not only one but two doses of the vaccine and had come down with rabies, so that while it may be of some value, I think that the value is not yet proven.

The question of two injections of typhoid vaccine came up. Personally, I have always felt that it was not so important how much vaccine you gave as the number of times you gave it. From experiments on animals, I should say that three injections were better than two.

Dr. O'Hara raised the question of measles blood. Inasmuch as practically every adult has had measles at some time in his or her life and doesn't have it again, that would seem to indicate that every adult has protective substances against measles in the blood. It is a perfectly rational method of treatment and can be used very easily. The blood, if necessary, can be preserved in sodium citrate.

Dr. Eastman spoke about the blanching test. The more I see of it the less I know about it and I confess I am not very sure of how to interpret it. We find that in testing our serum for potency we have to have a case in just the right stage, just the proper kind of rash, before we can get any results from it.

The question of autogenous vaccines came up. In the case of staphylococci, I think it makes little difference whether one has autogenous or stock vaccine. In the case of streptococci, I feel autogenous vaccine is much better, because with the streptococci you may get strain specific immunity and not general immunity.

Dr. Allen brought up the question of the intensity of the pseudo-reaction with the Schick. If the pseudo-reaction is intense, that person should be given small doses of toxin-antitoxin; otherwise, that person may have quite a severe constitutional reaction. So far as the administration of serum is concerned, the pseudo-reaction has no relation to serum hypersensitiveness.

Dr. Withington's question of quarantine I will refer to Dr. Scamman.

Dr. Bagg spoke of the high percentage of positive Schick tests in the nurses, and I presume that they are tested as they enter the hospital. It depends upon where your nurses come from. We found that something like fifty per cent. of all the nurses that we have tested are positive to the Schick test. That is a surprisingly high number. A great number of them are country girls from Canada, and it is now evident that only about one-half of this group possess natural immunity against diphtheria.

Dr. Ward spoke of an anaphylactic reaction following an injection of antitoxin in a person who previously had had toxin-antitoxin. It is impossible to give an opinion on that without knowing all the facts. To begin with, we don't know whether that person was naturally sensitive to horse serum protein. It may be possible that the toxin-antitoxin did sensitize that person so that an accelerated and aggravated case of serum sickness resulted.

Dr. Sisson spoke of the late administration of serum in scarlet fever. By the Dochez method you do get some anti-bacterial substance in the serum. It may be of value, but I would rather not say that it is of value.

Then the question of the use of smallpox vaccine in preventing whooping-cough. Only yesterday I found a reference in a recent paper in which some children had been vaccinated with smallpox vaccine at the time of a whooping-cough epidemic and those that had perfectly typical takes either had their cases of whooping-cough aborted or else very much mitigated by it. (Applause.)

The following officers were elected to serve for the ensuing year for the Section of Pediatrics:

Chairman, C. A. Sparrow, M.D., Worcester.
Secretary, Joseph Garland, M.D., Boston.

CHAIRMAN BLACKFAN: The Section of Pediatrics will now stand adjourned.

The meeting adjourned at eleven-twenty o'clock.

# AUTOLYSIS OF THE SPLEEN

BY SETH M. FITCHET, M.D., F.A.C.S., LAWRENCE WELD SMITH, M.D., AND AUBREY C. BENJAMIN, M.D.*

LITTLE is known about the blood-chemical, bio-chemical, or physiological changes *in vivo* or *in vitro* accompanying necrosis and autolysis of the human spleen.

Mason and Davison[1] have started what is primarily an experimental study of an animal's blood chemistry following complete removal of the spleen and the return of the organ to the abdominal cavity. They incidentally record macroscopic appearances at the autopsies of their animals. The abdomen usually contained 100-300 c.c. of brown-colored fluid, which they believed was not blood. There was a pseudo-fibrinous exudate on the abdominal viscera, which was easily removed, leaving a smooth and glistening surface. The intestines were congested and hyperemic. The spleen was less firm than normal, contained a gas, and was a dull green to bright green in color. There was a loss of weight, which implies a loss of size. The omentum was adherent to the spleen, hemorrhagic and discolored.

From their experiments, which are, at present, limited to too few animals to permit any sweeping conclusions, they cautiously postulate that in the *in vivo* autolysis of a sectioned spleen there are toxic substances produced which are lethal, the length of life depending on two factors: (1) the rate of liberation of the toxic material, and (2) the rate of absorption of the toxic substances.

They point out, however, that out of six animals three did not die following section of the spleen, and that in these three living animals there were no marked changes in the blood chemistry.

The following blood constituents were determined: (1) non-protein nitrogen, (2) amino acid, (3) uric acid, and (4) sugar. They do not specifically name the toxic material.

Corper[2], in a very careful study, has correlated the chemical changes which take place in the spleen undergoing necrosis and autolysis *in vivo* and, in order to avoid misinterpretation, *in vitro* also, with the histologic picture observed under the same conditions. In his historical resumé, from which I shall quote freely, Corper points out that there was practically nothing in the literature in the way of a comparative study of the chemical and histologic changes in an organ or tissue during autolysis or necrosis.

Weigert[3] describes the changes undergone by dead tissues.

Goldman[4] showed that a spleen kept aseptically in moist chambers at 37° C showed no macroscopic changes upon autolysis, but after 8 days the pulp cells showed changes, while the nuclei in the Malpighian bodies were well preserved. After fourteen days, the trabeculae were still distinctly differentiated from the pulp, and the nuclei of the Malpighian corpuscles were still retained, but in the remainder of the tissue the nuclei disappeared almost completely. Klebs[5] and Schmaus and Albrecht[6] have observed changes in other organs during autolysis and necrosis, but do not specifically mention the spleen.

Carriere and Vanverts[7], in animals, show that ligation of the splenic pedicle results in the death of the spleen, which becomes converted into an encapsulated mass of purulent and caseous material with proliferation inward from the capsule. This caseous and purulent degeneration they believe due to an innocuous colon bacillus, often associated with other harmless organisms, which they obtained from cultures from the spleen of all animals experimented upon, both before ligation of the pedicle and after the destruction of the spleen was complete.

Davidsohn[8] transplanted spleens into mice, and later found only pigment rests remaining.

Zervos[9] noted that spleens are absorbed in less than a year after transplantation. Lüdke[10] succeeded in transplanting a rabbit's spleen into the spleens of monkeys, and states that sections showed the included spleens well healed in.

Carrel[11] accidentally occluded a splenic artery in a dog, and noted that in about a year the spleen had entirely disappeared.

Wells[12] observed that splenic tissue, after being killed by heat (100° C), undergoes a very slow change in the body of a rabbit, being attacked only by invading leucocytes, while unheated spleen under the same conditions undergoes rapid autolytic changes.

Levene[13] and Schumm[14] have recorded observations on the changes occurring in the proteins and nucleo proteins of the spleen during autolysis.

Hedlin[15] and his co-workers[16] found two distinct proteolytic enzymes in the spleen. Leathes[17] notes certain substances as products of the action of the proteolytic enzymes.

Hasbroek[18], Coriat[19] and Meyer[20] have studied some of the changes produced by autolysis in the individual constituents of the spleen.

It will be noted in this historic summary that no mention is made of autolysis of the spleen in the human body.

Corper has used the largest dogs obtainable for a carefully planned and well executed study of the subject. He has determined and states the chemical composition of the normal spleen, and describes its microscopic appearance. Then, at definite intervals, both *in vivo* and *in vitro* he states chemical analysis and microscopic findings. For the detailed findings the reader is referred to his excellent article.

*For records and addresses of authors see "This Week's Issue," page 540.

Autolysis of the spleen *in vivo* in Corper's dogs, autopsied 2 days, 10 days, 20 days, and 40 days after ligation of the pedicle, may be summarized macroscopically as follows:

Two days after ligation of the splenic pedicle the spleen was of a greenish color, and soft in consistency. It could be handled and cut without disintegration. No mention is recorded of other abdominal findings.

Ten days after ligation in the second dog the autopsy revealed an adherent omentum, a thick reddish exudate in the peritoneal cavity. The spleen was found adherent to the posterior abdominal wall. It was encapsulated in fibrous tissue, which on section was shown to contain a greenish semi-liquid mass.

The third dog, autopsied twenty days after ligation, showed a reddish, congested omentum, a smaller amount of thick reddish exudate in the peritoneal cavity. The remnant of the spleen was in a mass of connective tissue, with omentum adherent to the mass. This splenic remnant was made up of a small amount of faintly reddish creamy liquid.

Forty days after ligation the fourth dog showed no exudate in the peritoneal cavity. The omentum was slightly congested. The splenic remains were completely encapsulated by a dense capsule, the interior of which contained a small reddish center.

In this same series of four dogs the microscopic findings are summarized as follows:

After two days the trabeculae could be differentiated from the splenic pulp, but all nuclei had disappeared. The surface of the capsule was invaded superficially by leucocytes, proliferating connective tissue cells, and probably by endothelial cells. In the deeper parts these cells were absent. The pulp was one mass of granular debris with occasional leucocytes near the capsule. In certain areas there were cells containing yellowish and brownish pigment.

The spleen, ten days after ligation, was a typical necrotic mass in which no nuclei were found. There was only a semblance of trabeculae and splenic pulp. There was no marked leucocytic invasion except at the periphery of the capsule, where there were a few leucocytes, connective tissue, and endothelial cells. The pulp was diffusely granular.

No microscopic findings are recorded for the third dog killed twenty days after operation.

The microscopic examination of the spleen of the fourth dog showed typical scar tissue. The connective tissue was irregularly arranged and was made up of spindle-shaped cells. Large pigment-laden cells with small nuclei and cytoplasm containing brownish-yellow granular pigment were noted. In one section of what appeared to be capsule of the spleen there was a more regular arrangement of the various types of connective tissue, and internal to this were a great number of large phagocytic pigment cells.

Microscopic examinations of tissues show chiefly superficial changes, in the main those connected with the cellular structure and arrangement and with the cell nuclei. Corper has rightly attempted to correlate these changes with his bio-chemical findings. His summary of this correlated study follows:

"The most marked chemical changes in a disintegrating spleen are noticed during the period when karyorrhexis and karyolysis are the characteristic features. When pyknosis alone is prominent almost all of the several constituents are in the coagulable or precipitable fraction, just as they are in the original normal tissue. After karyolysis is practically complete, the coagulable and precipitable elements of the tissue still gradually decrease in amount, but the rate is far below that occurring during karyorrhexis and karyolysis. Moreover, even when microscopical nuclear disintegration is practically at an end, the chemical process of disintegration is still going on, but very slowly. Finally, when nuclear structures can no longer be seen in the spleen, about 72 per cent. of the nuclein nitrogen, about 50 per cent. of the original insoluble phosphorus, and 70 per cent. of the original insoluble nitrogen, are still in the insoluble form (precipitable and coagulable by alcohol), while about two-thirds of the phosphated phosphorus remains in complex organic combinations."

Nowhere does Corper mention any toxic material, lethal or non-lethal, which might cause death from splenic autolysis *in vivo*, in dogs.

Parreira[21] reports a case of partial necrosis of the spleen, with adhesions to the great omentum, due to torsion of the pedicle.

This was in a woman 22 years of age, in whom a diagnosis of ptosis of the spleen had been made three or four years previously. In July 1922 this patient had symptoms of peritoneal irritation, pain and muscular rigidity, accompanied by fever. It was then noted that the spleen, which previously had been very mobile, had become fixed. A diagnosis of torsion of the splenic pedicle was made; however, all symptoms disappeared in about three weeks, except that the spleen was less mobile. Three months after this first attack she again had symptoms suggesting peritoneal irritation, and operation was decided upon, but postponed five weeks, because of bronchitis. At operation the spleen presented strong adhesions to the anterior abdominal wall, the small intestines, and the great omentum. On freeing the spleen it was noted the pedicle had twisted one and one-half turns. The spleen was removed. The patient made a good recovery.

Macroscopic examination showed a spleen 15x9.5x4 cm. normally shaped, weighing 300 grams. Externally there was a thick, opaque capsule which presented fibrous adhesions. The surface of the spleen was normal in appearance around these adhesions. The vessels of the pedicle were a twisted mass and the lumina were obliterated or filled with blood clots. A longitudinal incision was made through the convex surface towards the hilus revealing a yellowish white peripheral zone, just beneath the capsule, of unequal thickness. The deeper zone showed characteristic splenic structure with small hemorrhagic areas.

Microscopic examination: The capsule was thickened with lesions of the adhesive perisplenitis and

showed a zone of necrosis where the normal structure of the spleen was not found. This zone of necrosis was very extensive and contained only the remains of the connective tissue trabeculae. At the margin of this zone there were hemorrhagic areas with round cells filled with pigment. Following this there was a zone in which the true structure of the spleen could be seen. The follicles were not larger than normal and in some of them the artery presented a thickened wall and its adventitia was surrounded by a connective tissue ring showing hyalin degeneration. The reticulum in the splenic pulp in some places was a little thickened. The lacunae were elongated, filled with red cells and lined with unchanged endothelial cells. The trabeculae were in some cases thickened, in others they showed hyalin degeneration. In a section showing the great omentum, it was found that the vessels of the latter were numerous and dilated and some of them penetrated into the capsule.

Bartera[22] reports a case of total necrosis of prolapsed spleen from torsion of the pedicle.

This was in a woman 34 years old with a long history of malaria. For about four years she had had pain and swelling of the abdomen. The pain, which was not continuous, was first localized in the left hypochondrium. Four days before Bartera saw her she fell while doing her housework. After the fall the pain in her left hypochondrium, became intense, and was accompanied by vomiting, fever (100°), dyspnoea, great pallor, rapid pulse (160), and hippocratic facies.

Physical examination showed an enlarged abdomen, pain on palpation, and a large, smooth, hard tumor in the left lower quadrant. The normal spleen area was tympanitic.

A surgeon was called and agreed on a diagnosis of an enlarged, prolapsed spleen with peritonitis. Operation was deferred because of generally poor condition. She died three days after diagnosis.

At necropsy there was a large amount of serohemorrhagic fluid in the peritoneal cavity mixed with a few flakes of fibrin. The spleen was greatly enlarged and had prolapsed into the pelvis, compressing the rectum.

Macroscopic examination of the spleen showed a smooth, firm, elastic surface, brownish-red in color with clear spots. It measured 28 cm. x 18 cm. x 9 cm., and weighed 4 kilograms. The pedicle was 30 cm. long, and twisted twice on its axis. The vessels were much enlarged and thrombosed. The cut surface was smooth, variegated in color much like the external surface.

Microscopic examination: Splenic structure could not be recognized. Arteries and veins were thrombosed; around them there were more or less broken down erythrocytes and leucocytes. There was a great deal of leucocytic infiltration in the walls of the vessels and around them.

The case which is now described shows a remarkable arrangement of gastric carcinoma with secondary autolysis of the spleen.

The patient, age 54, had always been an active and vigorous woman; she had had six pregnancies, two children now adults, living and well. Seven years ago she had "some womb trouble" for which an operation was advised and refused. Six years ago she had "acute nephritis". Three years ago she had been "badly hurt by an auto". Three weeks ago she began having severe unexplained left upper abdominal pain and back ache, extending to the level of the left scapula. She thinks she has lost some weight. Bowels moderately costive. No genito-urinary symptoms. Five hours ago, for no apparent reason, she began to have severe lower abdominal pain and abdominal distension.

Physical examination showed a woman in great pain, (even though she had had morphine gr. ¼ prior to my seeing her), hippocratic facies, some dyspnoea, and mentally a little irrational. The heart sounds were irregular and weak, rate 120, and a loud blowing systolic murmur was heard over the precordia. The abdomen was markedly distended and tympanitic throughout. There was great complaint on even light palpation; tenderness seemed a little more marked on the right than left, and low rather than high. No masses or fluid could be made out. There was definitely more spasm in the right lower quadrant than elsewhere. The rest of the physical examination added nothing.

She rapidly failed and died eleven hours after the onset of this attack.

NECROPSY REPORT

*Peritoneal Cavity*

On opening the peritoneum a small amount of fluid is found which is somewhat turbid in appearance. The serosal surface is injected and roughened by a delicate fibrinous exudate. This is more marked in the dependent portions, particularly in the flanks and pelvis. The entire intestinal tract, but particularly the large bowel, is distended with gas. The appendix does not appear to be involved in the process primarily. The liver is adherent in part to the diaphragm and the mesentery.

The upper left quadrant of the abdomen is walled off by a rather dense mass of chronic inflammatory appearing tissue, so that it is impossible to determine the attachment of the diaphragm from the lower side. This wall of inflammatory tissue seems to leave an irregularly pyramidal space which is somewhat fluctuant on palpation. Careful search for the spleen in this area by dissection is unsuccessful, and a cavity is accidentally incised with the escape of about 200 cc. of brownish red, more or less brick colored, opaque fluid.

Further dissection of this region proves conclusively that the wall of inflammatory tissue represents the outer shell and capsule of the spleen, while the brick red fluid material is composed of autolyzed splenic pulp. The outline of the cavity roughly conforms to the usual arrangement and form of the spleen, complicated by dense adhesions to the regional tissues. The inner surface of this cavity is covered by a shaggy material suggesting an exudate.

On first opening the cavity the possibility of the fluid contents being a hemorrhagic purulent exudate was considered and cultures taken, which subsequently proved to be sterile. The cause of this unusual lesion of the spleen is found in the dissection of the pancreatic and splenic vessels, which are found compressed and obliterated by the extension of the tumor growth from the stomach to the colon and mesentery.

*LIVER:* Weighs 1075 gms. and appears to be of normal color and consistency. There are no metastatic nodules.

*PANCREAS:* Is firmly adherent to the posterior aspect of the stomach. It appears normal and is removed en masse with the stomach.

*KIDNEYS:* Each kidney weighs 100 gms. The capsules strip readily and on section appear fairly normal.

*ADRENALS:* Only the right adrenal is found at this time. The left is probably connected with the gastric mass which has been removed.

*GASTRO INTESTINAL TRACT:* The stomach is only slightly dilated. Upon opening the stomach a large fungating growth is seen to cover the entire lesser curvature, extending from a point one-half inch from the esophagus to a point one inch from the pylorus.

The esophageal orifice and the pylorus are not involved. This mass measures fully 6 cm. in width and projects into the lumen of the stomach as much as 2 or 3 cm. It is greyish pink in color, rather firm in consistency and has many large papillary projections. The lymph glands along the greater and lesser curvatures are enlarged and very firm. The duodenum is opened after it is removed from the abdominal cavity and appears normal except for a slight distention. The small intestine shows a moderate distention throughout. Otherwise it presents no pathology. The colon presents a marked distention in the proximal two-thirds. The descending and sigmoid portions are collapsed. At the splenic flexure a constriction of the colon is found which is due to the infiltration of the retro-peritoneal tissue and of the colon wall, itself, by a metastatic tumor growth. This constriction seems to be absolute and probably explains the patient's sudden and severe symptoms. The retro-peritoneal glands in the upper one-half of the abdomen are enlarged and firm and probably represent metastasis. The appendix is negative.

*GENITALIA:* The uterus is small and involuted. The tubes appear normal. The ovaries are small and fibrotic. The bladder presents a small amount of fibrinous exudate over its peritoneal surface, and is not removed.

*AORTA:* The aorta presents numerous atheromatous plaques and a slight amount of arteriosclerosis at the bifurcation.

MICROSCOPIC EXAMINATION

*LIVER:* This organ shows a moderate amount of central necrosis. There is also seen a beginning brown atrophy. The portal areas show an increase in the fibrous tissue element and some round cell infiltration. The sinusoids do not appear to be congested.

*SPLEEN:* Sections taken from this organ show an extensive fibrous tissue proliferation and in areas the picture is that of anaemic necrosis. Practically no normal tissue is seen. In places there is extensive round cell infiltration. In one area a small metastatic growth is seen.

*PANCREAS:* Sections through the head of the pancreas show no evidence of pancreatic tissue. However, there is seen a large lymph node which has been almost completely invaded and surrounded by tumor tissue. This presents the typical picture of a metastatic adeno-carcinoma. No pancreatic tissue has been included in these sections.

*KIDNEYS:* Present a picture of a beginning vascular nephritis. There is some cellular reaction in the glomerular tufts and the smaller vessels show some intimal thickening. In places the capsules are somewhat thickened.

*ADRENALS:* The sections show several pseudo-adenomata. The cortex and medulla appear within normal limits.

*GASTRO INTESTINAL TRACT:* Sections through the stomach wall present a typical picture of an adeno-carcinoma. The cells have an alveolar arrangement and are embedded in a connective tissue stroma. There is considerable invasion of the musculature and many areas of round cell infiltration. The section from the intestinal wall shows extensive infiltration of the serosa and muscularis. This represents a metastatic nodule which began to grow in the serosa, invaded, the muscularis and involved only a small portion of the mucosa. Here the tumor cells are embedded in a dense connective tissue giving a picture not unlike scirrhous carcinoma.

*OVARIES:* Section through the ovaries shows an extensive sclerosis and involutional changes.

*SUMMARY:* On reviewing the gross and microscopic pathology it is seen that the primary cause of death is due to this wide spread adeno-carcinoma involving almost the entire lesser curvature of the stomach. The distribution of the metastases is rather difficult to explain. One would ordinarily expect extension of this process to the liver and surrounding organs. The metastases to the small and large bowel are apparently due to direct extension. The nodule in the descending colon resulted in diffuse fibrous tissue proliferation with partial constriction of its lumen. No metastases to the liver were seen. The extensive changes seen in the spleen are apparently due to invasion and pressure of the splenic blood vessels causing anaemic necrosis and complete autolysis of its substance.

This reveals an extraordinary condition. This patient died of acute intestinal obstruction secondary to her carcinomatosis. With this almost symptomless carcinomatosis she had a complete autolysis of the spleen, which in itself gave remarkably few symptoms. Pain in the left hypochrondrium, radiating to her left scapula, of three weeks' duration, not severe enough to incapacitate her, even in the presence of extensive cancer, was her only complaint.

Cases of autolysis of the spleen are rare. Diagnosis of torsion of the pedicle of the spleen, the usual cause of autolysis, is extremely difficult, if not impossible.

From Parreira's, Bartera's and the above case it is noted that torsion may apparently be slow or rapid. If slow the symptoms are slight, if rapid they are severe. The spleen may enlarge because of interference with venous circulation. If there is prolapse of the spleen, as in Bartera's case, there may be rotation, and from the degree of rotation as noted by palpation, relative torsion of the pedicle may be suspected. If torsion of the pedicle takes place suddenly, as in trauma, there may be nausea, vomiting, violent pain, meteorism, rapid small pulse, and hippocratic facies.

Animal experimentation has given valuable information, but has not particularly helped in the diagnosis of autolysis of the spleen in man.

If diagnosis is made the treatment is, of course, obvious. Further animal experimentation may lead to a method whereby the condition may be diagnosed by blood-chemical, biochemical or physiological means.

In the few cases of necrosis of the spleen described in the literature the diagnosis has never been made.

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# AGRANULOCYTIC ANGINA—REPORT OF A CASE WITH RECOVERY*

BY TYREE C. WYATT, M.D.†

IN June 1927 Kastlin[11] carefully reviewed the 43 cases of so-called agranulocytic angina which had appeared in the literature before that time. He also reported two additional ones which had come to autopsy in the Toronto General Hospital. Since the appearance of that monograph a considerable number of cases have been reported in both the American and European literature. Although the classification of certain cases is extremely difficult, it seems justifiable at the present time to limit the term "agranulocytic angina" to those instances of throat infection with or without glandular involvement, which show a definite leucopenia, frequently below 1000, with marked decrease in the number of "granulocytes" or polymorphonuclear leucocytes. The following cases which seem to belong to this group have been reported since Kastlin's review: Hart[8] 2 cases; Finnegan[5] 1 case; Taddei[18] 1 case; Zikowsky[26] 4 cases which are included elsewhere; Dahlen and Wahlgren[4] 1 case; Koehler[12] 1 case; Vos and Staal[20] 1 case; Borchers[2] 1 case; Zikovsky[25] 10 cases, the details of which are not reported; Schultz[16] 1 case; Weihmuller[21] 1 case; J. Weiss[22] 2 cases with review of 92 other allied cases; Linthicum[13] 2 cases; Peritz[14] 1 case; Hirsch[10] 6 cases; Ashworth and Maphis[1] 1 case; Vos[19] 1 case; Zetterquist [24] 1 case; Gundrum[7] 1 case; Friedemann[6] 4 cases; Havercamp[9] 1 case; Whitehead[23] 1 case; Sachs[15] 1 case; a total of 42 cases, which, with Kastlin's review of 45 cases and the one reported here, make 88 cases found in the literature.

## CASE REPORT

The following case is reported because it is the first of this type admitted to the Peter Bent Brigham Hospital and because of recovery in spite of the exceedingly low leucocyte count, and without attempts at specific therapy aside from surgical drainage of the various localized areas of infection:

The patient was a single Irish woman, age 43, who was a ward maid in this hospital. Her family history, as far as she knew, was negative aside from the fact that one brother died of pulmonary tuberculosis at the age of 24 and one sister was said to have "chronic bronchitis." The patient came to this country from Ireland nine years ago, all of which time has been spent in Boston, and for the past six years she had worked in this hospital. She had had only the usual childhood diseases. Her history since childhood had been entirely negative with the exception of having been sick with influenza for three weeks in 1920, and having waited on her brother who died of pulmonary tuberculosis.

*Present Illness:* During the two or three weeks preceding the acute present illness the patient said that she had realized that she did not feel as well as usual, having considerable headache almost all the time and tiring more easily than usual. During that period she had had several skin infections in the form of furuncles on her hands and face, none of which had required surgical treatment. Two days before admission to the ward she had first noticed a sore throat and on the following day discovered a tender lump under the left jaw. She had rather marked headache on both days and felt feverish but had continued at her usual duties as maid.

The *physical examination* showed nothing of importance aside from the condition of the throat and neck. The tonsils and whole pharynx were diffusely reddened and edematous with small patches of grayish exudate on the right tonsil. In the left submaxillary region there was a firm tender mass about 1.5 × 2 cm. without redness of the skin, which was presumably a lymph node, although it was in the region of the submaxillary salivary gland. In the right submaxillary region there was a lymph node about 1 cm. in diameter which was non-tender. There was no other lymphatic enlargement.

*Temperature, pulse, and respiration:* The temperature at the time of admission was 101.8, rising on the fourth day after admission to 103.6, and during the remaining ten days on the medical ward before transfer to the surgical ward continued to fluctuate irregularly between 98.6 and 101.8. The pulse rate varied between 90 and 120, tending to be between 100 and 110. The respiratory rate was between 20 and 25.

*Blood findings:* The admission blood examination showed Hgb 70%; R.B.C. 4, 100,000; W.B.C. 1800; differential count, polymorphonuclears 2%, small lymphocytes 30%, large mononuclears 68% (in all probability a number of these cells were large cells of the lymphocyte series). The leucocyte count gradually came down in the daily counts until it reached a low level of 700 five days after admission. The differential count at this time showed 5% polymorphonuclears and the remaining cells seemed definitely to belong to the lymphocyte series. From this point the count gradually came up, reaching 1400 on the ninth day after admission, with 26% polymorphonuclears; and four days later 2800 with 61% polymorphonuclears. At the latter examination two nucleated red blood cells and two myelocytes were seen. There was no noteworthy change in the erythrocyte count.

*Progress of the throat and neck infections:* During the first week after admission the infection in the throat continued with the formation of exudate on the left tonsil similar to that on the right and with marked edema of the whole pharynx. Smears and cultures from the throat showed no evidence of diphtheria bacilli, organisms of Vincent's angina, or fungi. Numerous streptococci, staphylococci, and

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large Gram-positive bacilli were present. During the first four or five days after admission the swelling in the left submaxillary region enlarged, became quite tender and then began to subside. During this time there was rather marked prostration, and the prognosis seemed to be quite poor. On the eleventh day after admission she was seen by a surgical consultant who advised continued hot applications; two days later there was definite fluctutation and she was transferred for drainage. Her throat at that time showed definite improvement, but there was still some purplish discoloration and edema. She continued to be considerably prostrated and the outcome seemed quite questionable. In addition to the submaxillary mass she had developed, about a week after admission, one or two slightly enlarged, tender lymph nodes in the left axilla, and two days before transfer to the surgical ward an area of tenderness, redness and induration appeared just below the outer half of the left clavicle. A blood culture taken on the day of transfer was negative.

*Summary of the surgical record:* On the day of transfer the left submaxillary abscess was opened and about an ounce and a half of thick yellowish pus was obtained. It could not be definitely established whether the point of origin of the abscess was in the salivary gland or not; however, the cavity was in close proximity to the gland. Cultures from the pus showed numerous staphylococci and hemolytic streptococci. On the second day after transfer the subclavicular abscess was drained. Cultures from this pus showed only streptococci which were slightly hemolytic. After the last drainage the temperature became normal for three days and the patient was much more comfortable except for a cough which had developed after transfer. The leucocyte count, which had been 2800 on the day of transfer, was 4500 four days later with 54% polymorphonuclears. It remained between 5400 and 7400 at the time of discharge, with essentially normal differential counts. The cervical and infraclavicular wounds were healing satisfactorily, but a week after transfer she began to complain of pain in the left axilla and on examination there was considerable diffuse brawny induration. This induration continued with developing redness, until the area was opened a week later. This culture showed Gram-positive bacilli which were diphtheroid in type. Her temperature again returned to normal and the induration markedly subsided, but the wound was still draining slightly at the time of discharge, after thirty seven days on the surgical ward and fifty-one days in the hospital.

*Follow-up since discharge:* The axillary wound healed satisfactorily. She felt perfectly well six weeks after discharge, having resumed her duties in the hospital. Her blood at that time was entirely normal. There was still slight induration in the region of the operation scars, most marked in the axilla. The general physical examination was otherwise entirely negative. She had had no sore throats since discharge.

## COMMENT

As one goes over some of the reports in connection with so-called agranulocytic angina or agranulocytosis and monocytic angina or infectious mononucleosis, the probable relationship of the two types of cases is definitely suggested. Schenck and Pepper[17] and Cottrell[3] have already called attention to the similarity of some of the cases and to the difficulty in the diagnosis between the two types and acute lymphatic leukemia, particularly in the aleukemic stage. The extremes are quite different in their blood pictures, but in between the extremes there are numbers of cases with varying degrees of leucocytosis and leucopenia and varying abnormal differential counts, which are very difficult to classify and which suggest that all are atypical reactions or lack of reaction on the part of the blood-forming organs to different degrees or types of infection. It is interesting to think of the blood picture of typhoid fever and certain other diseases in this connection. Future studies and observations in these cases may throw some light on the factors which determine the type of atypical reaction. The cases reported seem to warrant no conclusion as to etiology. All sorts of pyogenic organisms have been recovered from the throats and other areas of infection. The cases with positive blood cultures have tended to show streptococci or Friedlander's bacilli. The bacteriologic findings in the case of this report certainly were not conclusive, different organisms being found in the various areas of infection. Most writers seem agreed that the disease is primarily an infectious one; however, they are not agreed as to whether it is primarily a throat infection with secondary invasion of the blood stream in some cases or whether it is primarily a blood stream infection with late infection of the throat. Schultz's case[16] suggested the latter. It is striking that in a very large number of cases it is mentioned definitely that the patients had not felt entirely well for some time prior to the acute illness. This suggests the possibility of a low-grade infection of some sort being active for some time before the more acute infection and that this in some way may be a factor in the unusual blood picture.

On the other hand, Vos and Staal[20] suggest that the disease is primarily one involving the leukopoietic function of the bone marrow, with late infection of the throat. Friedemann[6] also does not agree that it is primarily an infection but suggests that it originates in some endogenous disturbance, possibly of endocrine nature. The four cases of his report were treated with roentgen irradiation over the long bones, with recovery.

Attempts at specific therapy have included blood transfusions, anti-streptococcic serum and roentgen radiation over the long bones. The reports of beneficial results from any of these lines of treatment as yet seem inconclusive. The treatment of the case of this report was only symptomatic aside from the surgical drainage of the various abscesses.

## SUMMARY

A total of eighty eight cases of so-called agranulocytic angina has been reported. There are a number of cases of throat infection and atypical blood pictures which suggest the probable relationship of the above cases to so-called monocytic angina or infectious mononucleosis. The case of this report belongs definitely in the agranulocytic group. In addition to the throat infection there were localized infections in the left

submaxillary, left infra-clavicular and left axillary regions. The bacteriologic findings in all of these areas were inconclusive. The blood culture was negative. The only treatment, other than symptomatic, was surgical drainage of the abscesses. The patient has entirely recovered, with return of the blood picture to normal.

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# A CONTRIBUTION TO THE STUDY OF WOMEN IN MEDICINE

## Were There Qualified Women Doctors Before the Nineteenth Century?

BY KATE CAMPBELL HURD-MEAD, M.D.*

MUCH controversy has been going on recently among medical historians over the question whether there were women graduates in medicine before the nineteenth century. The man historian, with a patronizing smile, says, "But you know, there never were schools for women doctors before the nineteenth century". He admits that some women might have been trained in midwifery after a certain manner, but he assures us that the famous medical women of Salerno had no real existence, that the famous Trotula was a man masquerading under a woman's name (for what reason he fails to say), and that our useful "Old Dame Trot" was only a myth of nursery days along with Old Mother Hubbard.

Stung by these gibes the woman historian goes to the great library and begins a systematic research among the medical books of long ago only to find a great dearth of original material either by men or by women, and a vast number of works copied from Galen or compiled and translated from a few other writers without giving credit to the original author. Hippocrates himself possibly copied from earlier writers and from the case records on the Esculapian temple walls, but he copied so wisely and added so much valuable material from his own records that his work has stood *facile princeps* for nearly twenty-five hundred years. Galen copied from Hippocrates and from his other predecessors as well as from his own contemporaries, adding descriptive anatomy and many wise observations of his own, and, as a rule, honestly giving credit to the authors from whom he quoted, including several women doctors who seem to have been as well trained as he for the practice of medicine.

There are many proofs that from the beginning of time women were quietly and efficiently tending the sick, and binding up wounds (even Homer says so,) and that they not only cared for the sick women and children, gathering herbs and compounding medicine, but often then, as now, acted as referee in regard to cosmetics and all legitimate beautifiers of the body. "That school-girl complexion" was as much appreciated among the ancient Assyrians, Egyptians, Greeks, and Romans, as in the twentieth century, and to have a fine skin seemed as important for man or woman as to have a healthy body and active mind.

Although few men or women who wrote medical books appear to have signed them with their own names or, perhaps, the copyist forgot to insert the name of the author, the silent witness of the tombstones shows that many women doctors were in practice in ancient Greece and Rome. Not only their husbands and patients but the general public thought it worth while to commemorate them by a monument when their work was finished. In the "sacred ways" near Athens there have been found many Greek inscriptions such as, "To Basile, the Woman Doctor", and "Thecle, the Woman Doctor, lies here". The same is true among the Romans. In Ostia and many other cities of Italy, in the Rhone Valley and in far-away Spain and Africa, has been found many a marble slab erected to a woman doctor by some grateful patient. In Merida, near the Spanish-Portuguese border, is a marble slab bearing this inscription:

| | |
|---|---|
| Juliae Saturninae | To Julia Saturnina. |
| Ann. XXXXV | Age forty-five years. |
| Uxori Incomparibili | Incomparable Wife. |
| Medicae Optimae | Best of Doctors. |
| Mulieri Sanctissimae | Most Holy Woman. |
| Cassius Philippus | Cassius Philippus. |
| Maritus, Ob Meritis. | Her Husband, (erects it) on account of her merit. |

Among the women doctors whom Galen mentioned and from whom he frequently copied was a certain Antiochis, of the second century, A. D.,

*For record and address of author see "This Week's Issue," page 540.

whose statue has been discovered in the ancient town of Tlos. On it is written, "To Antiochis, Daughter of Diodotus, of Tlos; the council and commune of the town of Tlos, appreciating her medical skill, raised this statue to her at their own expense."[1] Galen also mentions Aspasia, a doctor of his own time, from whom he copied many prescriptions, and Cleopatra, a famous gynecologist, another of his colleagues, from whose books, in fact, everybody copied, generally without mentioning her name.

For thousands of years there must also have been Egyptian women doctors. They were not only midwives and priestesses but surgeons and healers who practiced like men with and without magic. In the great archeological museum in Berlin any sightseer may examine the medicine chest of Queen Menthuhotep which she carried on her journeys for the benefit of her patients just as a modern woman doctor carries a Boston bag of remedies. This medicine chest, now some three thousand years old, was buried with the queen for use in the next world. It contained jars of ointments, counter-irritants, dried herbs to be made into medicines, small spoons and scales for measuring powders, and a few little instruments all evidently selected with care.

Religion and medicine were everywhere closely united in pre-Christian days, and we find women as well as men officiating in the temples and devoting their lives to healing the sick. In the Greek temples the goddess Hygeia's help was more often sought then that of her father, Esculapius. She generally assisted her father besides ministering to diseased minds, teaching people the rules of healthy living, and comforting those in sorrow. He was a surgeon, and though the tales of his skill are quite impossible to believe they were vouched for with great assurance. Such testimonials to the surgical skill of Esculapius were by order carved in marble and placed outside the walls of his temples. Among them are found tales like these: "I had dropsy. The doctors could not cure me. I came to the temple and slept. The god had pity on me. He cut off my head, hung me up to drain, replaced my head, and I woke in the morning cured." And, "I had a great worm in my body. I slept, and the god put his hand down my neck and removed the worm. I was cured immediately." And another, "I had a great sore on my body (cancer?). The god cut it out while I slept and there were blood spots on the floor when I awoke, cured." For operations and treatment not only Esculapius but also Hygeia and the priests received certain fixed fees; the sacred snakes also had their cakes and the temple dogs their bones. The prescribed ritual of the preliminary bath, the incubation or temple-sleep, the offerings, etc., are too long for insertion here, but they can be found in recent books on the cult of Esculapius. In most of the votive reliefs, however, Hygeia seems to have been equally as much adored as her father.

How it happened that women of Christian times, after having been free to study and practice medicine like men for probably thousands of years, came to be down-trodden, silenced, hidden in their homes, in fact veritable slaves for centuries, is difficult for us to understand, but there is no lack of proof that secretly or even against the law they were continuously acting as doctors, nurses, and midwives, during all those years. Their condition of apparent servitude began during the decadence of Rome while the church of the Christians was growing under man-made laws and priest-ridden regulations. As the material world was to be exchanged after death for the spiritual world, it was evident that the greater the torments of this life the more glorious would be the reward in the hereafter. Therefore neither men nor women in general thought it worth while to try to better their earthly conditions or to ward off death by new methods of curing disease. The health of even the most robust was undermined by malaria, plagues, famine, wars and persecutions, but these trials were borne with Christian resignation as among certain Hindus today. Probably the women also suffered from too frequent child-bearing, glandular defects, lack of nourishing food, and mental depression, and they may have become apathetic because of the conditions surrounding themselves and their families and so they lacked energy to take up the cudgels in their own defense. If a person in our day becomes obsessed with an inferiority complex, he or she is an easy mark for those who have the superior complex, subsequently the "*descensus Averni facilis est*".

In the pre-Christian life of the Hebrews woman had no such inferior position. It was the early Christian Fathers who believed that "a woman without reproach was as rare as the phenix, the gate of iniquity, the dart of the scorpion". Tertullian said, "Because of *you* the Son of God was killed". A council of the church, in A. D. 581, decided that women were not reasonable beings and priests and deacons should not live under the same roofs with them. The Council of Metz confirmed this. The Council of Trent reaffirmed it, and yet we find St. Jerome praising the practical medical work of many women, and writing in most friendly terms of Fabiola about the hospitals she was building and the patients she was treating. Other saintly women were also caring for the lepers and outcasts in the early days of the Church, even in the far-away Holy Land. Doubtless they did nearly all of the midwifery and most of the compounding of remedies according to the rules of Galen and Dioscorides, learned perhaps from tradition if not from actual books. If they wrote medical books none have as yet been found.

There came to be, however, another side to the story. In the later medieval years, when the cult

of the Virgin became the public cult of woman in general, chivalry came into existence. What a relief it must have been to a young girl to find herself the object of adoration of some handsome knight! Could she, the heroine of the poet and story-teller, be actually the wicked Eve, or was she not to be exalted like Mary, the mother of Christ? Was she a temptress or was she a saint? Was she fit for a pit or for a pedestal?[2] Even Albertus Magnus debated seriously whether or not the Virgin Mary knew the *Seven Liberal Arts* and decided in the affirmative, for

> "Ne hadde the appil taken ben,
> The appil taken ben,
> Ne hadde never our lady,
> A ben hevene quene."

In every-day life, however, it made little difference whether a woman was Eve or Mary. The Wife of Bath, who had had five husbands, told the Canterbury Pilgrims that every night she had to listen to stories about "wicked wyves" taken from Ovid, Tertullian or Saint Jerome, and she adds:

> "For trusteth wel, it is impossible
> That any clerk wol speke good of wyves,—
> But if it be hooly Seintes lyves,—
> Ne of noon oother womman never the mo."

Those were the days when, in spite of chivalry, any man had the right to beat his wife (even William the Conqueror, took advantage of this right on more than one occasion), and from childhood girls had a monotonous existence and were governed by fear rather than by love. If they were rich, they were married at the age of fifteen and childhood was over, or else they entered a convent for life. In either case their remaining years were full of responsibilities with few diversions.

As we have already surmised there was no wide diffusion of learning in the Middle Ages. In fact learning was not even a gentleman's accomplishment and therefore to a certain degree it was left to the women. Few of the nobility or even barons could read, though the common people sometimes went to school to the "mass-priests" for a short time.[3] Before the twelfth century the "Seven Liberal Arts" constituted the sum total of knowledge for all except the most erudite. This consisted in the study of grammar, rhetoric and logic, followed by arithmetic, geometry, music, and astronomy. Not before the twelfth century was any specific medical science taught and then anatomy was taken verbatim from Galen, the treatment of disease from Dioscorides, and gynecology directly or indirectly from Cleopatra. Sudhoff says that, in accordance with the Christian teachings of the Middle Ages, it was not thought proper for a man to treat women's diseases, and as monks were not allowed to study or teach gynecology, it was left to the midwives to teach each other by a sort of catechism taken from Soranus. He had copied most of his material from the works of Cleopatra, the contemporary of Galen, whose name had been forgotten for centuries. Israel Spach[4], in the prologue to his late sixteenth century translation of her books says of Cleopatra, "O daughter most brilliant, would that I might have had the pleasure to translate thy work more worthily."

But, as Diepgen says, we are not to think that clever doctors did not exist in those ages simply because they did not write, and it was fortunate for woman-kind that there were women midwives and gynecologists to help them in their time of travail and pain. Wright (op. cit.), tells us again and again that the ladies of the medieval household were both nurses and doctors. Medical men were not often at hand to be consulted in the sick room, and therefore the sick and wounded were necessarily turned over to the mistress of the household for care. Welch[5] gives us an account of a day's routine of such a mistress. The watchman sounded his horn at sunrise, she rose from her curtained bed, stood on a fur rug before the fire to bathe and dress, said her prayers, and then, after a bowl of soup, she made a tour of the estate or village to visit the sick and injured, prescribe for them, or dress their sores. In a French manuscript of the thirteenth century Roger of Parma mentions such a woman who set a broken limb as well as a man. She also bathed the wounded knight, soothed the nervous woman by sweet songs, diverted a fretful child, read the latest romance to a love-sick youth, or rushed off to deliver a mother of her new baby. Then occasionally, if time permitted this woman doctor might go hawking, play a game of chess, read Virgil with a tutor, entertain the wandering minstrel or guest, or else turn to her loom and weave the cloth for a dress. Besides all this she had the oversight of the servants and housekeeping, the buying and selling of the produce, and thus she filled a round of busy days. Her life vividly reminds us of the everyday life of the woman doctor of today.

In many of the old romances we find ample confirmation of this ability of women to do the medical work of their times when their husbands were off at war, or suffering at home from terrible wounds. Priests were discussing theology, monks were too busy copying manuscripts to visit the sick, and slaves were working on the farms. Therefore, while magicians and astrologers were studying the heavens to cast horoscopes and find the causes of disease and the ways of the Devil, it was left for the women to do whatever their hands found to do for the poor, the sick, and the afflicted. The stories of Queen Radegonde, and of Queen Elizabeth of Hungary, as they did medical work among the outcast, show why the women who worked so hard in practice had no time for writing books. Unfortunately, even the famous abbesses who superintended great monasteries, managed hos-

pitals for lepers, penitentiaries for prostitutes, and lying-in homes for the poor, though they may have accumulated a great deal of useful knowledge about diseases, had no time for writing medical books.[6] We know, however, that the famous Abbess of Fontevrault, at the time of Richard the Lion Hearted, and also the sister of Abelard, and the nuns of Paraclete all studied and taught whatever was then known of the treatment of disease and of wounds, and if so many of the monasteries had not been sacked or burned, we might be able to reconstruct the libraries of these women doctors of the Middle Ages. Singer[7] tells us that only fourteen medical works written between the ninth and fourteenth centuries have been found, and they contain no new material, being merely translations from the Greek into poor Latin. As for the drugs in use during those years, their preparation was quite bound up with the belief in demons and spirits. Herbs, steeped or merely ground, plucked by night at a certain stage of the moon like the mistletoe or hauled out of the earth by dogs like the famous mandrake, were used to appease evil spirits, for the science of medical treatment was not yet born.

All sorts of animal extracts, even excreta, were used in medicine. Many minerals and metals were dissolved or worn as amulets to cure certain diseases. Precious stones were thought to be in sympathy with the stars and worn for luck, or they were supposed to be endowed with sensations and human instincts and cared for accordingly. Neuburger[8] tells us that in India more than seven hundred different plants were in use as medicine, among them aphrodisiacs, poisons and antidotes, sleeping remedies, and pain relievers. Theriac, one of the commonest drugs in the Middle Ages, had been invented by one of the physicians of Nero. It contained several scores of medicinal substances including vipers' flesh, and it is still to be found on the shelves of the apothecaries in remote country districts of as modern a nation as France.

In the Middle Ages as we have already noted many a widow and unmarried girl took refuge in a nunnery where she learned how to read the Bible, write, sew, sing hymns and tend the sick. Catherine of Pisan, when a widow, not only supported herself and her children by writing poetry but also several books in praise of the work of women. Saint Hildegarde, at the head of a monastery, wrote the most famous books on medicine of her time, the "Causae and Curae" and the "Physica". These medical books contained the diagnosis and treatment of most of the known diseases of men, women, and children, and they were used and copied for centuries. Among other noted women who wrote books and tended the sick were Theodosia, mother of St. Procopius, Blanche of Castile, St. Catherine of Siena, the Blessed Angela of Foligno, Roswitha, a nun of Gandersheim, in the Hartz Mountains and Mechthild, of Magdeburg, a mystic, who had studied magic and had visions of healing; there were others, perhaps less religious, like the famous medical women of Salerno.

Having, therefore, shown the conditions of living and the state of education, medically, in the greater part of Europe during the Middle Ages, and noting that women did the largest part of the medical and surgical practice, we may now turn to that famous school at Salerno, where, in the tenth and eleventh centuries, there was really a medical school worthy of the name where women as well as men taught, wrote and practiced medicine and surgery. This great school may possibly have been an offshoot of the Benedictine Monastery at Monte Cassino, near Naples, but more probably it was formed like many of the early medical schools of the United States by a group of scholars, clever practitioners probably, who enjoyed teaching and writing, as also the emoluments thereof, and so, for various reasons, had attracted pupils from all over the known world.

Salerno was a large city in the eleventh century. Merchants from everywhere touched at its coast in trade; pilgrims to and from the Holy Land, crusaders and warriors, stopped there for rest, food, and merchandise. A certain Robert, of Normandy, brother of William the Conqueror, landed there in 1098, and having been cured of a poisoned arrow's wound, he built a great Norman church by way of thanks, and a castle on the hill for a watch tower, walled the city, erected convents and houses for pilgrims, and hospitals for the sick to which, in after years, the Knights of St. John as well as the Benedictine nuns added larger hostels and infirmaries. The medical school had already been established before the time of Robert, and women doctors, as well as men were teaching the students. These men and women were already so famous that Robert asked them to write for him a compendium of medicine. This compendium was called the Regimen Sanitatis which begins, "Roberto regi scripsit Schola Salerni".

During the Great War Dr. Pietro Capparoni, who was stationed at Naples, had the opportunity to examine several hitherto unpublished manuscripts which he found in Salerno, among them a certain *Who's Who* of the eleventh century containing the names Trocta, or Trota, Gariopontus, Roger, and Roland perhaps the actual persons who wrote new medical books in Latin, not merely copies of Galen or compilations from old writers. Trocta's was called the Trotula; Roger's Rogerina; Roland's Rolandina; etc.*

*It was suggested by Mazza, in the sixteenth century, in his history of Salerno, that the great quartet of Salerno were Gariopontus, who wrote on surgery, mainly from Galen; Petronellus, the little Peter, who wrote on internal medicine; Trotula, on gynecology and obstetrics, and Roger of Parma, whose great book on surgery is signed and dated 1180. The combined works of these four writers were used by Guy de Chauliac in the fourteenth century, not only in his classes at Montpellier, but in his own famous book on surgery. No doubt has been expressed as to the authenticity of any of these writers except in the case of the woman Trotula, and therefore it seems unreasonable to doubt hers alone.

Although few traces of its ancient grandeur can now be seen, and nothing is left of its famous university, Salerno's background of wooded hills, its distant volcanoes, its terraced vineyards, its blue bay, its sadly defaced cathedral, and its steep, narrow streets, make it one of the most picturesque of Italy's sea-side towns. As a medieval city, however, it was quite magnificent, delighting the hearts of the hundreds of students who gathered there. Arabs, Jews, Normans, French, English, all went to Salerno to study as to a Mecca of learning. It was not until long after the founding of the University of Naples that the fame of Salerno began to dwindle, its libraries were burned, and finally, in 1811, by decree of Napoleon, the school ceased to give diplomas, and consequently ceased to exist.

Happily, however, the monks of Monte Cassino had copied its precious manuscripts, some of which were found in the library at Breslau by De Renzi, and others may perhaps yet be found in other parts of Europe. In one of these manuscripts is a picture of the birth of the great Tancred, son of Robert of Normandy. The mother lies on a long bed under a green coverlet, her blonde hair falling over a red pillow. Two women doctors seem to have been officiating at the birth of the baby. They wear long gowns of green and yellow and look very high-born and important. One of them holds the baby high in her arms for the mother to see, and the whole picture gives us a touch of tender family life and medical feminism which is quite undisguised even in the somewhat archaic painting.

The title doctor in the middle ages meant simply teacher; it was first given as a medical title at Salerno two hundred years after the days of Trocta who had been called *magister, master* or *"Maestra Trotula"*. Besides this a medal was struck in her honor showing on one side the legend, "Medendi Arte perita" and the face of a gracious woman, on the obverse a jar of poppies, the key and staff and serpent of Esculapius, and the words, "Salerni nata, florunt ann. XI."[9] It is thought that this Trotula, or Trocta, was the wife of a certain Platierius, related to the Cophon family, among the most important families in Salerno. She is supposed to have married into the Ruggiero family, (she is often called Trotta de Ruggiero), but the name was a rather common one for centuries. In 1097, about the time of the writing of the *Regimen Sanitatis,* a certain Ruggiero, lord of the castle of Montuori, left a donation for his "mother Trotta". Matteo Ruggiero perhaps another son, also speaks of Trocta, his "mother," and of his "father, Giovanni," both of whom, he said, wrote on the "Cure of Disease". It is also said that for two hundred years their descendants were medical teachers and writers. Matteo says of his mother that she looked after sick women as a *"Maestra"*, not as an empiric; and he recalls her treatment of uterine colic by the application of sweet or spicy odors to the nose. De Renzi, (Vol. I, p. 150), and Mazza both believe strongly in the authenticity of the medical works attributed for so many centuries to this Trotta. De Renzi says, "Multae doctrinae matrona Salernitana, quae librum scripsit de morbis mulierum et earum cura, et alterum de compositione medicamentorum."

There is no doubt that the women of the eleventh century preferred to be treated by women if possible. We read of one whose disease had been diagnosed as vulval hernia or rupture. "Trotula vocata fuit quasi magistra operis," and on examination she diagnosed the condition as an abscess. This must have been a rather famous case for Constantine, the African, who taught in Salerno somewhat later, reported that Trotta lanced the abscess, dilated the opening with two fingers, evacuated the pus, directed the nurse to keep the wound open for drainage, and then to heal it with medicated oils. Whatever treatment she ordered seemed to her contemporaries very practical, and to us it seems far in advance of her times. Her book *"De Morbis Mulierum et eorum Cura"*, is full of useful hints for the relief of painful symptoms. She recommended mud baths, warm sea-water baths and hot compresses for certain abdominal congestions, gave advice as to infant feeding during the teething period, ordered sweatings for the relief of renal dropsy, cataplasms and counter-irritants for pain, gave poppy juice for sleep, calculated the date of convalescence in malarial fevers and surgical operations, attended carefully to the diet, suggested the lighting of fires if the house seemed damp, sprinkled the patient's face with sweet-smelling extracts, applied oil of roses and violets to suppurating sores, and cleansed the mouth with syrup of flowers. She was careful not to allow the patient to overwork during convalescence, nor even to tire herself by over-talking; she suggested suitable music and interesting games, and was careful never to give an unnecessarily gloomy prognosis. Her final salutation was always, "Vade in pace, Christo duce."

It can not be denied that these details seem more like those of a woman doctor than of a priest or monk who was anxious to get back to his cell to consult Galen for the treatment of the case, according to a fixed rule of procedure. When Trotula examined a patient she was most thorough and particularly careful not to overlook any detail that might have a bearing on the diagnosis. She says, "As soon as you reach the patient ask where the pain is, then how severe it is, then feel the pulse and test its character, see if there is any fever, ask if there has been a chill and when, and if the pain is worse at night, watch the facial expression to determine the amount of suffering, feel of the abdo-

men to find whether it is soft or rigid, inquire as to urination, examine other parts of the body for tender spots. It you find nothing of consequence ask what other doctor has seen the case and what his diagnosis was, in order to find out if this was the first attack of the kind. Finally, at the end of the examination Trotula says, "having found the cause it will not be difficult to find the cure".

One of the important chapters in the Salernitan Compendium is Trotula's article, *"De Mulierum passionibus"*. Some of the titles discussed are *"De modo generationis embrionis"*, *"De sterilitate ex parte viri"*, *"Ut mulier concipiat"*, *"De provocatione menstruorum"*, *"De fetus morte"*, *"Ad fistulam mammillae"*. She described uterine polypi and hydatid mole, showed that she had some knowledge of syphilis, and had excellent chapters on the treatment of obstetrical complications and gynecological operations. For example, she says, "As a result of a difficult labor the perineum sometimes ruptures its entire length, the vulva and anus making one opening through which the uterus may drop and then become indurated and ulcerated. It should be treated in the following way; first, apply to the uterus compresses of hot wine in which is plenty of butter, (butter was more common in those days as a salve than a food); after the uterus has become soft it can be replaced very easily. Close the opening with three or four deep silk stitches, and press firmly against the perineum thick linen compresses saturated with tar water to avoid odor. Then use a dusting powder between the patient's legs, place her feet higher than her head and keep them high for eight or nine days. Give her care and diet she needs, but do not bathe her until the wound is healed. Do not let her cough or eat indigestible food."

Many of the early chapters of the Compendium have been lost, perhaps as many as twelve. (DeRenzi Vol. II.) Articles have been referred to by later writers as if written by Trotula such as one on pleurisy, one on stone in the kidney, another on surgical diseases of the abdomen, in all of which specially intelligent reasoning and observation seem to have been shown.[10]

George Sticher[7], says that most of the surgery of Salerno was very modern. For example, they lifted the opposite side of the skull in trephining after a blow on the side of the head. They removed abdominal tumors, tied the saphenous vein, used an anesthetic of poppy juice and deadly nightshade inhaled from a saturated sponge, expected healing by first intention after using antiseptics of hot wine, placed their patients in the Trendelenburg position when necessary, and took all precautions against secondary hemorrhage.

There are a few fragments of another anonymous work, perhaps by Trotula, containing articles on epilepsy, eye diseases, ear-ache, the gums and teeth, how to excite vomiting, etc., but as most of the thirty-five articles in the Breslau codex are unsigned it is difficult to be sure of their authorship. They are, however, easy reading and full of interest, written in the style of modern case-records, though physical charts and modern tests are, of course, lacking. Ordericus Vitalis therefore, was doubtless right in calling Trotula *"una sapiens matrona,* deserving as well the fame of tradition as of her contemporaries".

That Trotula was not free from some of the superstitions of her time may be seen by her ready rule for the diagnosis of sex in the unborn baby. She says, "Take a few drops of the mother's blood or of milk from her right breast, put them into water, and if the milk or blood sinks the child will be a male". This method of diagnosis was frequently quoted after her time, and even Constantine, the African, with scientific Arabic medicine at his finger tips, did not refute it.

The faculty of the school at Salerno, in the eleventh and twelfth centuries, seemed seriously to feel that they were marking an epoch in medical history by emerging from strict adherence to the words of Galen, and writing carefully from their own observations as to the diagnosis and treatment of disease. One of their books was called *"Practica brevis,"* another was *"De Aegritudinum curatione"*. In both these books the famous remedies of the women doctors are faithfully quoted, among them being prescriptions for the hair and complexion, for dysuria, hemorrhoids, vaginal discharges, etc. Among the remedies we may note the vapors of antimony for bronchitis, and the use of aloes steeped in rose water for erysipelas of the face.

Somewhat later than the eleventh century a long didactic poem was written purporting to be a versified copy of the *Regimen Salernitate,* an attempt to make a sort of encyclopedia of contemporary medicine. This poem has 842 lines. It is concerned with gynecology, pregnancy, abortion (whether from accident or design), the conduct of labor, the dead fetus, surgery of the prolapsed uterus, paralysis of the bladder, etc., evidently based on Trotula's work. There are also various additions by the poet-author. There is another poem of 526 lines on diseases of the skin purporting to be by Trotula. This poem was written to tickle female vanity, for among the topics we find these: the removal of superfluous hairs from the face, the treatment of pimples, the use of hair dyes, red, black and yellow, and of coloring for the cheeks, the care of the lips and teeth, prescriptions to cure dandruff, mouth washes to sweeten the breath, and lotions to remove the odor from the arm-pits. Doubtless these are practical subjects but they are not in the professional style of Trotula's gynecological writings.

Another anonymous medical poem, discovered by Littré in 1852, has 6322 lines, divided into seven books, of which the first and second

contain many of the suggestions of Trotula, though not in her style and of a much later date. It has been suggested that the poem is a mere forgery, or perhaps written by William of Saliceto, or copied from Copho and Arnold of Villanova, but the Salernitan school had by that time lost prestige, quacks and charlatans had taken up the works of the learned professors, and as usually happens in such cases, honest students were forced to seek other medical schools.

A Latin jingle has come down to us from this period which in English is as follows:

> "Calls himself doctor and fool
> Jew or Monk, actor, barber, witch,
> Whether alchemist or massagist,
> Or bather or falsest oculist,
> Where gold is the object
> Art and virtue perish."

To recapitulate, then, it seems fairly well proved that the *Compendium Salernitatum*, found in Breslau in 1846, and the "new collection" found by Capparoni in 1918, both show that the medical school at Salerno had been organized in the eleventh century as a reaction against the medical crudities of the preceding centuries by a group of brilliant physicians at a time when Norman princes and crusaders and merchants from all over the world were in the habit of calling at this well-known port in search of provisions or homes. Not being a religious institution, the wives and daughters of the professors were allowed to study any of the courses and those who were proficient became teachers and writers. Later Salerno became a famous center of Arabic medicine, where many medical books were translated from the Greek and Latin into Arabic, and in their turn were retranslated into Latin, stored in out-of-the-way-places, and thus saved from fire and ruin.

Although Mazza was unable to trace any specific Trotula in the records, owing to the fact that her name was a common one, he found the names of several other later woman doctors, teachers, and midwives, such as Constantia, the midwife, who died in 1308; Helena, who was professor of Hebrew in the twelfth century; Laurea Constantia Calenda, 1423, daughter of a doctor, Salvatori, who was a teacher both at Salerno and at Naples, a "noble woman of great erudition"; and Abella, Mercuriadis, Rebecca, Sestia Guarna, all of whom were celebrated for their medical writings. Abella wrote a metrical treatise on *Black Bile, and the Nature of Women.* Mercuriadis wrote on the *"Crisis in Fevers".* Rebecca wrote on the *"Urine".*

Before closing this account of the medical women in the Middle Ages it would be pertinent to ask when the title doctor of medicine was first used, and what was the course of study necessary for a degree. The Charter of the University of Paris, in 1270, answers this question; it reads as follows:

> "A candidate for a degree in medicine must have heard the Ars Medica twice in regular course and once in extraordinary course, with the exception of Theophilus on Urines, which it is sufficient to have heard once; the Viaticum twice in regular courses, the other books of Isaac, the Arabian, once in regular course, twice in extraordinary courses, except the particular diets, which it is sufficient to have heard in extraordinary or regular course; the Book of Antidotes, of Nicolas, of Salerno, once. The verses of Egidius, of Corbeil, are not required. The student should read the books on Theory, by Ali Ben Abbas, and on Practise, sometimes attributed to Constantine, the African. He should swear that he has done this study honestly. . . . If a doctor has been convicted of perjury or lying, even though licensed, he may be degraded.[11]" Then, in order to become licensed, the Master under whom the bachelor has studied must testify to the Chancellor in the presence of all the masters called together for this purpose, concerning the suitability of licensing the candidate who must have successfully passed his examinations during the five and one-half or six years of his study.

There was no dissecting, there were no patients to be seen, no experiments to be proved. It is therefore, small wonder that the universities were not crowded with medical students or that women could hardly take the time for such an education when practical work lay at their doors, and oral teaching at the bedside could be had easily. Midwifery was entirely left to women. Blood-letting was not permitted to the clergy, and consequently women and barbers were taught to do minor surgery. Herb gathering and the preparation of medicines was the duty of every housewife, and it was she who had to be ready to bind up the wounds of the men who were injured in war. Miss Power[2] says that they learned their medical knowledge by reading aloud the books written by Trotula and quizzing each other. Because of jealousy they were not allowed by law to practice beyond the walls of their own estates, though this rule was often disobeyed.

We therefore come back to find our first question answered. There certainly were women doctors before the nineteenth century, and their education compared favorably with that of the men of their times. As for the reasons why for fifteen hundred years women in general submitted to take a lower position in the intellectual scale than men we may confess that although they may have been hypnotized into the belief in their own inferiority and the hopelessness of being able to change their status we believe that men also suffered from the same inferiority complex inasmuch as they had not learned that comradeship and co-öperation with women is far more beneficial than rivalry and that there could be a new order of things better than that of their fathers.

Perhaps, as Kipling says, it was not yet time either for women or men to waken and use their full powers for it was not yet the dawn of a new era.

> "So, when all the world is asleep and there seems
> no hope of her waking

Out of the long, bad dream that makes her mutter and moan,
Suddenly all men arise to the noise of fetters breaking,
And everyone smiles at his neighbor and tells him his soul is his own."

*(The Dawn Wind.)*

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## "TRENCH MOUTH", OR VINCENT'S INFECTION

Vincent's infection, or "Trench Mouth", was first noticed about 1897, and has undoubtedly been more or less endemic since that time. It was not until the World War, however, that the disease took on epidemic form. In France, during that war, the condition, given the name of "trench mouth", at that time, was more common than were typhoid and malaria during the Spanish-American War. It was quickly recognized by the dentists with the troops; but, owing to the cramped living conditions in which the troops lived, it continued to spread. Many soldiers wth infections of the mouth and pharynx were sick in hospitals and in quarters. Since the World War it has seemed to spread slowly through the States, or perhaps has been more promptly recognized.

Vincent's infection may present itself in the mouth or as Vincent's angina in the throat, or the two may be present together. It is believed to be due to the combined action of two varieties of the same germ. Inflammation and the formation of ulcerative areas of greater or less magnitude, located on the mucous membrane of the gums, cheeks, tongue, and tonsils are characteristic of the disease.

The milder or more common form is slower in its progress and remains on the surface, not affecting the membrane deeply. Stagnant, foul mucus or serum seems to be necessary to its successful development. Undoubtedly the true type is more often found in unclean mouths where decayed teeth are present, around spaces where faulty fillings overhanging gum margins are a source of irritation as well as uncleanliness, or where the soft tissues of the mouth have already received injury from diseases such as pyorrhea, salivation, or other diseases.

The infection is carried and spread from an infected individual to a well one by direct contact. Eating utensils not properly cleaned, face towels, drinking cups, personal articles, kissing, and living in crowded buildings without plenty of fresh air and sunshine are some of the causes of the spread of this disease. The exact mode of transmission has not been entirely agreed upon by all authorities. An unsuspecting person may be a carrier and transmit the organism, harmless to himself but harmful to others.

To prevent the likelihood of infection with this disease everyone should keep his mouth in a clean, healthy condition. When teeth first begin to decay, they should receive immediate attention, and the small cavities should be filled without delay. No decayed teeth or broken-down roots should be allowed to remain in the mouth. The mouth should be thoroughly cleaned by the use of a toothbrush and dental paste or powder, or even soap or salt and water, after each meal, if possible; but in any case always before retiring for the night, and the first thing on arising in the morning. The gums should be properly massaged with the toothbrush or the fingers, and the roof of the mouth and the tongue should be softly brushed also. Although it might be possible for a clean mouth to become infected, the chances are greatly in favor of a person with such a mouth, for a clean mouth with healthy vigorous gums and mucous membrane will resist infection. The throat is extremely difficult to cleanse properly, but always before retiring a gargle of salt water or any mild antiseptic should be used.

The true diagnosis of Vincent's infection can be made only in a medical or dental laboratory with the use of the microscope. Whenever the uncomfortable symptoms of a persistent sore mouth are experienced, that person should immediately consult his dentist or his physician for treatment. Vincent's infection cannot be treated at home with household remedies. In the first place, it could not be properly diagnosed, and the danger of its becoming acute, with serious after-results, would be great.

In case a dentist or a physician is not available, the treatment should be the use of a mouth wash at frequent intervals until skilled treatment can be obtained. Undoubtedly the mico-organism causing this disease cannot live or keep its virulent nature in the presence of air or free oxygen. Although it might continue to exist for some time in the presence of oxygen, it will not multiply. It is evident, then, that any oxygen-liberating compound will check the growth of these organisms. For this purpose there are three outstanding drugs which may be used as an efficient mouth wash. They are hydrogen peroxide, potassium permanganate, and sodium perborate. All of these drugs, when freshly prepared, liberate oxygen.

Hydrogen peroxide is a solution easily obtained and is capable of liberating 10 volumes of oxygen. When used as a mouth wash, diluted with equal volumes of water and used at frequent intervals, forcibly working it back and forth in the mouth by contraction of the lips and cheek muscles, it will serve very well as a temporary measure.

Potassium permanganate in 1:5,000 dilution is good, although it has a disagreeable taste. Sodium perborate is a white powder readily soluble in water, and when freshly dissolved liberates about nine per cent. oxygen. It is a good home remedy, but will not keep in solution and will lose strength in solid form if kept in a warm place.

Any of these remedies will serve as a temporary expedient for a few days until the services of a dentist can be secured; but it is dangerous to delay treatment if it can be possibly obtained.

During the acute stage the toothbrush should not be used, as it is likely to cause a hemorrhage by forcibly removing the diseased membrane. This would furnish more pabulum for bacterial growth.

Although the outlook in Vincent's infection is favorable and the condition usually responds quickly to competent treatment, neglect may result seriously, as the micro-organisms causing this disease have been isolated from other more serious diseases such as meningitis, peritonitis, and diabetes. Most cases of Vincent's infection can be cured with proper treatment.—*United States Public Health Service.*

Case Records
of the
Massachusetts General Hospital

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICO-PATHOLOGICAL EXERCISES

EDITED BY R. C. CABOT, M.D.

F. M. PAINTER, A.B., ASSISTANT EDITOR

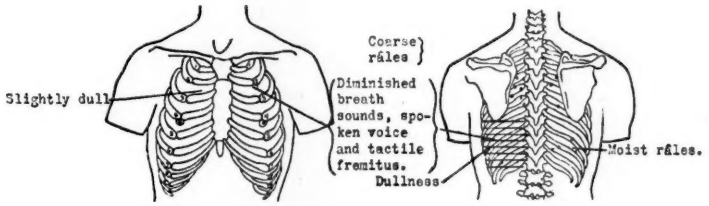
## CASE 14301

## COUGH, FEVER AND DYSPNEA FATAL IN THREE DAYS

MEDICAL DEPARTMENT

An Irish-American schoolgirl fourteen years old was brought to the Emergency Ward April 28 too ill to give any history.

The persons who brought her in said that she had been perfectly well until three days before admission, when she "caught cold". The following day she woke very ill, with cough, fever and rapid respirations. The day of admission she was worse. She was so ill that only a slight examination was done in the Emergency Ward.




The leukocyte count was 14,000. She was taken as soon as possible to the medical wards. There she did not appear to have a chance of living more than an hour or two. Her pulse had risen from 150 in the Emergency Ward to 180. She was cyanotic about the lips and finger tips. Her respirations were not however extremely labored. She presented the picture of extreme toxemia rather than anoxemia. It was thought unwise if not futile to disturb her with attempts at oxygen administration, so she was given fluid by mouth, codein and morphia and let strictly alone for the night.

On clinical examination the following day she appeared as before. The respiration was rapid, with grunting expiration and dilating of the nostrils. Her eyes had a wild look. The lips and tongue showed a thick white coat. The skin was dry and hot. The lung signs were as shown in the diagram. The heart, blood pressure and abdomen were normal. The heart was not displaced. The pupils were normal. The reflexes are not recorded.

The urine is not recorded. Blood examination in the ward showed 10,800 to 3,000 leukocytes, 78 per cent. polymorphonuclears, hemoglobin 90 per cent., reds 4,800,000, smear normal. Blood culture showed no growth.

The patient was put under an oxygen tent. After about forty-five minutes her color was thought to have improved somewhat. She lived about an hour longer, dying at noon the day following her admission.

### DISCUSSION

BY RICHARD C. CABOT, M.D.

#### NOTES ON THE HISTORY

This is an extremely rapid course,—all this in three days and in a child who was at the age to resist disease almost as much as at any age.

It is splendid treatment, I think—the kind we do not see enough of—the treatment of letting very sick people alone and not taking away their strength by extensive clinical examination.

#### NOTES ON THE PHYSICAL EXAMINATION

There were the signs of pleural fluid rather than of solid. But fluid in the ordinary serous form cannot make a person as sick as this. So I am in doubt what those signs mean. Although they sound a good deal like fluid I am inclined to think they are due to pneumonia.

They believe she had pneumonia and tried to save her by putting her in an oxygen tent.

#### DIFFERENTIAL DIAGNOSIS

I do not see what we can say but pneumonia. It is perfectly possible we are wrong. I have seen a case just like this die of acute anterior poliomyelitis when everybody was thinking of something in the lung. But we have not a bit of evidence.

If it is pneumonia then that leucocyte count of 3,000 will be especially interesting, because we have long believed that while a high white count in pneumonia does not give a good prognosis, a low and especially a falling white count means a bad prognosis. Here it was never high and it went down very low, a bad sign in any infectious disease that I know.

This is certainly an infection. Could it be miliary tuberculosis? I think so. But we cannot do more than guess at it without a history of some other form of tuberculosis previously observed, bones, glands, genito-urinary, etc. It may have been there, because we got no good history. But I should say pneumonia is more probable.

This case came at the period when there have been a number of necropsies showing influenza pneumonia. Last week at the Brigham Hospital Dr. Wolbach said of a pneumonic lung that he

had not seen anything that looked so much like that since the days at Camp Devens. I am wondering whether this is not pneumonia of the influenzal type.

CLINICAL DIAGNOSIS (FROM HOSPITAL RECORD)

Lobar pneumonia.

DR. RICHARD C. CABOT'S DIAGNOSIS

Probably pneumonia.
Possibly miliary tuberculosis.

ANATOMIC DIAGNOSES

Staphylococcus aureus septicemia.
Multiple septic infarcts of the lung.

DR. TRACY B. MALLORY: This case was a total surprise, and is in part still unexplained. It is a case of staphylococcus aureus septicemia of a very fulminating type, with huge infarcts in the lung that grossly simulated lobar pneumonia. One of the infarcts included almost an entire lobe. The source of the infarcts was entirely undetermined. There is nothing in the story to suggest an injury. We were not allowed to open the head, so we cannot answer on the question of ears. Ears or sinuses seem by all odds the most likely thing. There was nothing in the pelvic veins or in the legs as far down as the knees.

DR. CABOT: With the wisdom of hindsight we can say that was extraordinarily short for pneumonia. We should have been more suspicious, because she lived only three days in all. But even if I had suspected that it was not pneumonia I certainly should not have expected that it was infarct from staphylococcus septicemia, because I never heard of such a thing. It is brand new in my experience. Did we have a blood culture?

DR. MALLORY: There was one during life, but it was negative.

DR. CABOT: Then they did not neglect anything there, and with that culture negative I do not see how any human being could have made the diagnosis.

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## CASE 14302

## THE VALUE OF DEFINITE LOCALIZATION OF ABDOMINAL TENDERNESS IN ACUTE UPPER ABDOMINAL PAIN

SURGICAL DEPARTMENT

A married Irishwoman fifty-seven years old entered March 13 complaining of pain in the upper abdomen and back of five days' duration.

The onset was at eleven o'clock in the morning on March 9, a sudden very sharp pain in the midepigastrium. It remained localized chiefly in the epigastrium, with some radiation to the right upper quadrant and slightly less severe pain in the right back at the angle of the scapula. She had nausea, sweating, and a temperature of 101°. The pain was steady, not colicky, and lasted until four p.m., when it was entirely relieved by morphia. The evening of the following day it recurred, as severe as before, and persisted until admission except when relieved by morphia. She had four doses in all, the first two with complete, the second two with partial relief. On the second day of the illness she induced vomiting. For the first two days she was jaundiced and her urine was very dark, though her stools were normal. The jaundice had disappeared in the last two days. For four days she had taken only liquids because of almost constant nausea. Her bowels had moved daily with enemas. Previous to this illness they were regular. At admission she had fairly severe epigastric and right upper quadrant pain and constant nausea.

Two sisters had diabetes.

Except for a few infections not relevant to the present condition the patient had been well and strong all her life until three years before admission. Then she had two attacks similar to the present one, lasting two or three days, associated with jaundice and requiring morphia for relief. During the past six months she had lost a few pounds.

Clinical examination showed a very obese woman with flushed face lying in bed apparently in no great discomfort. Chest expansion limited. Lungs hyperresonant throughout. A moderate number of crepitant râles at the right base. Well marked tenderness across the upper abdomen from the gall-bladder to the left costal margin. The tenderness was just as marked on the left as over the gall-bladder. No masses or spasm. (The patient had had morphia a short time before the examination.) Possibly very slight pitting edema of the left ankle and lower leg. Scars of old septic knee, right. Pupils and knee-jerks normal.

Before operation amount of urine not recorded, cloudy at both of two examinations, specific gravity 1.010 at both, rare leukocytes in the sediment at both. Blood not recorded before operation except 24,400 leukocytes. Icteric index 5. Stools not recorded.

Chart before operation normal.

An internist found the patient an excellent risk for any type of anesthesia,—the arteries, blood pressure, heart and lungs all normal.

March 15 operation was done. It was followed by drainage of about five ounces of bile daily into a bottle and only a small amount into the dressing. March 18 the urine showed sugar and the blood sugar was found to be 372. A diabetic régime was started. The next day the blood sugar was down to 62. After March 26 Benedict's test was always blue. Bile continued to drain at the rate of five ounces daily. March 27 the stools were brown, the chart flat. By March 29 all the wicks were out except part of one. April 2 there was still profuse drainage from the incision on the right and a little from the incision on the left. The blood sugar was still high, but not so high as before. For the

next two days there was no biliary drainage. April 10 the patient was discharged relieved.

## Discussion

BY DANIEL FISKE JONES, M.D.

Dr. Cabot said in starting the discussion of his case in the July 5 number of the NEW ENGLAND JOURNAL OF MEDICINE, "We go wrong [in discussions of reported cases] on lack of a good history more often than we do on lacks in the physical examination." I would like to repeat this for emphasis. On the other hand, this particular case shows the great value of a very accurate examination of the abdomen.

The important points to be noted in the history of this patient are:

(1) A previously healthy, obese woman.
(2) A sudden onset of steady pain across the epigastrium.
(3) Temperature normal except on the fourth day, when it rose to 101°.
(4) Pain constant in upper abdomen and back for six days previous to operation.
(5) Persistent nausea, but little vomiting.
(6) It was said by the family that she was slightly jaundiced before entering the hospital. Icterus index in hospital normal.
(7) Bowels moved every day.
(8) A history of two previous attacks similar in every way to this one.

The points of importance in the physical examination were:

(1) Definite and marked tenderness across the upper abdomen, no more marked over the gall-bladder than at the *left* costal border.
(2) Temperature and pulse normal after entering the hospital.
(3) Leukocytosis of 24,400.

In attempting to make a diagnosis we must consider those conditions which cause a sudden onset of severe constant pain across the upper abdomen. Among the more important may be mentioned cholelithiasis, cholecystitis, pancreatitis, perforation of a peptic ulcer, appendicitis, obstruction of the small intestine, diaphragmatic hernia through the esophageal opening, and many would include renal calculus and hydronephrosis.

It is impossible to exclude cholecystitis, cholelithiasis and pancreatitis on the symptoms as given above.

Perforation of a peptic ulcer rarely occurs without a previous history of indigestion. There is occasionally an acute ulcer which perforates without previous symptoms, but in perforations we expect a sudden severe onset with collapse, a rigid abdomen and death within forty-eight or seventy-two hours. Occasionally an ulcer perforates and walls off without causing a peritonitis. The patient then has pain and tenderness localized in the upper abdomen, usually with temperature. If the infection remains localized, the pain gradually disappears. This patient was not seen until the third day and may have had evidence of a perforation on the first and second days. The pain in this case persisted for six days. In addition to this, we have a history of jaundice in two previous similar attacks as well as in this one. Such a condition would not be expected with a perforated ulcer.

Appendicitis can be excluded on the ground that the pain persisted in the upper abdomen for six days, while in appendicitis it rarely remains localized there more than a few hours. The tenderness in our patient extended across the upper abdomen, with no tenderness any other place in the abdomen. Jaundice would not be present unless there were a pylephlebitis or sepsis, and it would then be persistent and not clear up in two days as it did in our case.

Small intestine pain is referred to the epigastrium, but in obstruction of the small intestine a careful history helps out. In such cases the pain is always intermittent and usually severe in the first few hours; later the pain becomes constant. In obstruction, vomiting would be a prominent symptom, not nausea. There would be no jaundice. Tenderness would be present over the distended bowel close to the obstruction. A patient with small intestinal obstruction would be in a serious condition in less than forty-eight hours and would not live six days. The bowels would not move every day as in our case.

Diaphragmatic hernia may cause a sudden onset of epigastric pain, but vomiting would be a prominent symptom and only the food or water recently swallowed would be vomited. If the pain and vomiting persisted, early operation would be necessary. There would be no tenderness across the upper abdomen, and there would be no jaundice.

It is often stated that epigastric pain may be due to renal colic, but it has been our experience that it rarely occurs. The tenderness would be localized over the kidney and at the costovertebral angle and there would be none across the upper abdomen as in our case.

With the above conditions excluded, it will be seen that we are left to make a differential diagnosis between cholecystitis, cholelithiasis and pancreatitis. Cholelithiasis must be considered seriously, for we have a sudden onset of severe epigastric pain with nausea and jaundice and a history of two similar attacks three years before. The condition one would expect to find would be a stone impacted in the cystic duct so close to the common duct that a partial obstruction of that duct was produced, or a stone in the common duct and one blocking the cystic duct causing distension of the gall-bladder. The only reason for suspecting a cholecystitis is the continued severe pain and a temperature of 101° on one occasion. The tenderness over the gall-bladder might be due to a distended gall-bladder or a cholecystitis. But the tenderness was not only

over the gall-bladder; it extended across the abdomen, and it was as marked at the left costal border as over the gall-bladder.

There is one condition which could cause all the symptoms and physical findings, that is, acute hemorrhagic pancreatitis. The sudden onset of pain in the epigastrium and the persistence of a constant pain across the abdomen and into the back with persistent nausea are very suggestive of pancreatitis. Slight jaundice is frequently present. But the physical findings are far more important, for the symptoms might be caused by a distended gall-bladder. The tenderness extending across the upper abdomen from the gall-bladder to the left costal margin is characteristic of pancreatitis and is rarely found in any other condition. This finding with symptoms suggesting a cholecystitis will almost always make a correct diagnosis of pancreatitis.

The temperature in pancreatitis may be normal for the first twenty-four hours, but after that it usually ranges about 100°. The leukocytosis of 24,400 is difficult to explain, as in pancreatitis it usually ranges in the neighborhood of 15,000. The one count made may have been due to a temporary rise or an error. Other examinations might have given us lower counts.

The sugar found in the urine and the increased blood sugar have no relation, we believe, to the pancreatitis. Of the cases at the Massachusetts General sugar was never found in preoperative examinations of the urine. There is, I believe, no evidence to show that patients with diabetes are any more liable to acute pancreatitis than normal persons. To cause sugar to appear in the urine there must be an almost complete destruction of the pancreas, and if that occurs death usually takes place within a few hours. Sugar does appear in from one to ten years in those cases in which there was an extensive destruction of the pancreas at the time of the attack. The statement that two sisters had diabetes has no significance we believe. Persistent nausea with little vomiting has been present in a large percentage of pancreatitis cases.

The statement that the bowels moved every day with an enema seems to be rather against the diagnosis of acute pancreatitis, when we consider that the diagnosis of intestinal obstruction was frequently made in these cases a few years ago, and was the diagnosis made on the last case seen by me.

PRE-OPERATIVE DIAGNOSIS

Subacute cholecystitis and pancreatitis.

OPERATION

Gas and ether. A paramedian incision was made. The gall-bladder and bile aspirated from it appeared to be normal. The pancreas was very much thickened and indurated throughout its entire extent, averaging at least two inches in diameter. There were many areas of fat necrosis over it and in the gland itself. The base of the transverse mesocolon was infiltrated and contained many areas of fat necrosis. The same picture presented through the gastrohepatic omentum. The gall-bladder seemed to have no relation to this condition, as there was no evidence whatever of an inflammatory process in or about it. The capsule of the pancreas was incised, broken up, and three cigarette wicks were inserted, one brought through a stab wound to the left of the midline, the other two through the incision. The gall-bladder was drained by a rubber tube. The wound was closed in layers.

FURTHER DISCUSSION

The operation brings out a few points. The gall-bladder was normal in appearance, and even if there was a slight infection, it is probable that it was in no way responsible for the pancreatitis, in spite of statements which have been made to the effect that acute pancreatitis is frequently caused by cholecystitis. Recent work has shown that there is no lymphatic connection between the gall-bladder and the pancreas, and no one has yet produced an acute hemorrhagic pancreatitis by infection from the gall-bladder. If we believe in the work of Archibald, which seems to show that pancreatitis is due to regurgitation of bile into the pancreatic duct, the gall-bladder should be drained to relieve any pressure in the common duct. This was done.

While Archibald does not approve draining the capsule of the pancreas or the pancreas, we believe that it is of value, that it relieves the patient at once of the pressure in the retroperitoneal space about the pancreas and in that way relieves the pain and we believe tends to prevent further destruction of the pancreas and retroperitoneal tissue.

To make a diagnosis of acute pancreatitis one must make a diagnosis of cholecystitis from the history, and then by careful examination find definite tenderness extending to the left of the midline.

DIAGNOSIS

Acute hemorrhagic pancreatitis.

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## TRYING IT ON THE CONSUMPTIVE

IT would seem that man has tried every permutation and combination of chemistry and cookery, has exhumed the buried secrets of alchemy, searched far and wide for new and precious elements, pored over the pages of the Chinese pharmacopoeia and has revived the Doctrine of Signatures in the hope of finding a medicine for phthisis. We recall, out of many, a venal snake venom cure; a scorching chlorine inhalant, ozonated this and that, nauseating messes of fats and oils, calcium in a hundred forms, iron in a thousand combinations, copper and gold, colloidal and otherwise, to be taken by mouth, inhaled, rubbed on the skin, injected under the skin, into muscles and into the veins. They present altogether an amazing array and where they did not actually harm the patient they often diverted him from the usual hygienic treatment and frequently left him impoverished. When the chemist discovered that coal-tar could be made to yield an almost limitless variety of compounds, the retorts and funnels ran fast, the chemist experimented with new linkages, new substitutions, the pill and pellet machines pressed and punched as never before and the dyeing vats were emptied into bottles bearing cryptic names and seductive labels, and the end apparently is not yet.

A glance through one single issue of the *American Review of Tuberculosis* reveals man's ingenuity and industry in devising drugs, christening them and then trying them on the consumptive. These are some of the names under which the preparations are paraded, "Gomenol," "Krysolgan," "Triphal," "Aurophos," "Ipecopan," "Helpin," "Lipatren," "Collosol," "Proflavine," "Geodyl," "Omnadin," "Dilaudid" and "Sanocrysin." Then, in the same issue there are abstracts of reports on the use of autogenous vaccines, of Vandremer's vaccine, of living virulent tubercle bacilli, of X-rays, ultra-violet light, oleo-thorax, actino-therapy, helio-therapy, of treatment with the homelier salts of iodine, calcium and antimony, with cod liver oil, ethyl morrhurate (to increase the lipases) with camphor, hypertonic dextrose solutions and insulin. The organotherapists have also had their try but they used only spleen extracts instead of their favorite gonadal and thyroid and pituitary preparations. These treatments are only those that are mentioned in this one issue. It would appear that the consumptive is not being neglected, at least experimentally. We wonder, however, if these treatments are always carried out along with and not sometimes substituted for the accepted recuperative regime.

We would not have it appear that we are without hope that some day out of all these trials will come a remedy to relieve the distress and speed the healing of the lesions of the tuberculous. But, we do want to warn of the danger that some of our readers may be misled by the lure of new names, or by their urgent desire to find something that will accomplish the unusual. There is no specific drug for tuberculosis. The most that we can expect of medicinal agents at present is that they may alleviate pain, reduce the intensity of the cough, stimulate the appetite and aid the digestion, and we have already many well-tried drugs for these purposes. Special proprietary preparations are no better than the prescriptions that any physician can write. But, until our chemists and pharmacologists can give us something better, let us rely on earlier diagnosis, rest and then more rest, fresh air, good food and as peaceful a state of mind as we can secure in these days.

## LEE PREFERS ITS MILK RAW

NINE HUNDRED cases of septic sore throat with some forty deaths were due, this summer, to milk from an infected cow in Lee, Massachusetts. This milk was distributed and consumed in a raw state. It is safe to say that had it been properly pasteurized not a case of the disease would have resulted. The lesson is obvious; whether or not it has been learned is still a question but the indications are that another sad

failure of the human mind to work on a logical basis is at hand.

Past experience must lead us to believe that the writing on the wall is ignored; that he who runs will not read. Other communities have suffered from similar epidemics and it has taken repeated experiences to drive home the fact that an ounce of prevention is worth a pound of cure. So far, according to frequent information, one pasteurizing plant has been installed in the vicinity of Lee since the epidemic, and no regulations have been passed regarding the pasteurization of milk. As far as Lee is concerned it has returned to the status quo ante epidemicum, confident in the false assumption that lightning does not strike twice in the same place.

The Department of Public Health is doing all that is in its power to prevent a repetition of Berkshire County's recent disgrace, and has obtained an appropriation to provide for a six months' milk inspection demonstration in that county. The cost to the county will be nil. Two meetings have been held with members of the boards of health of the county and the interest expressed has been slight. In the words of Dr. Bigelow, a great indifference is descending on the Berkshire people who want to forget the matter as soon as possible. An effort is now being made to arouse the health boards and the physicians of the county to co-öperate in this project. If the effort fails it will be dropped, the appropriation will return to the Treasury, and public health will receive another setback from the public which it seeks to protect.

We are not, after all, living under conditions of benevolent despotism; we cannot force the people to bow to any measure even if designed for their welfare, for ours is a government, presumably, of the people. The best that we can do is, by enlightenment, to try and create a public opinion, and the public mind is curiously opposed to the simplest types of education. It is through the physician of the state that this enlightenment may eventually be accomplished. Will they do their part in creating a demand for the universal pasteurization of milk?

## THE COMMONHEALTH

*The Commonhealth,* the quarterly bulletin of the Massachusetts Department of Public Health, contains in its issue for the second quarter of this year a valuable symposium on rabies. The treatment of and prevention of the disease is described in an article by Dr. Milton J. Rosenau, the laboratory diagnosis is considered by Langdon Frothingham, M.B.V., of the Department of Comparative Pathology at the Harvard Medical School, an article on canine rabies has been contributed by Dr. Hugh F. Dailey of The Angell Memorial Hospital and Dr. George H. Bigelow, Commissioner of Public Health, and Frank B. Cummings, formerly Director of the Division of Animal Industry, have expressed themselves on rabies control in Massachusetts.

Rabies continues prevalent in eastern Massachusetts; four persons have died from it in the last two years, and hundreds have been forced to take the prophylactic treatment. Every effort must be made to awaken in the public a consciousness of this present menace.

## THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

WHITE, BENJAMIN. Ph.B., Ph.D. Yale, Director, Division of Biologic Laboratories, Department of Public Health, Commonwealth of Massachusetts; Assistant Professor of Bacteriology, Immunology and Preventive Medicine, Harvard School of Medicine and Harvard School of Public Health; Honorary Member Massachusetts Medical Society and Fellow American Academy of Arts and Sciences. His subject is: "Serums and Vaccines in the Prevention and Treatment of Infectious Diseases—A Critical Review". Page 505. Address: 375 South Street, Jamaica Plain, Mass.

FITCHET, SETH M. A.B., M.D. Harvard, 1921. F.A.C.S. Junior Assistant Surgeon, Children's Hospital; Assistant in Surgery, Massachusetts General Hospital; Associate Surgeon, Baptist Hospital; Instructor in Surgery, Tufts; Assistant in Orthopedic Surgery, Courses for Graduates, Harvard. Address: 270 Commonwealth Avenue, Boston. Associated with him are:

SMITH, L. W. A.B., M.D. Harvard, 1920. Assistant Professor of Pathology, Harvard Medical School. Director of Research, Boston Floating Hospital; Pathologist, New England Deaconess and Baptist Hospitals. Address: 240 Longwood Avenue, Boston. And

BENJAMIN, AUBREY C. M.D. Harvard, 1921. Address: 35 Eleanor Street, Chelsea, Mass. They write on "Autolysis of the Spleen". Page 521.

WYATT, TYREE C. A.B., M.D. Syracuse University, 1922. Instructor in Pathology, Syracuse University College of Medicine 1922-1924; Assistant Professor of Pathology—ibid 1924-1927. His subject is: "Agranulocytic Angina—Report of a Case with Recovery". Page 525. Address: 721 Huntington Avenue, Boston.

HURD-MEAD, KATE C. M.D. Woman's Medical College of Pennsylvania, 1888. Medical Director, Bryn Mawr School, Baltimore, 1890-1893; Consulting Gynecologist Middlesex County Hospital; Vice-Pres. Connecticut State Medical Society, 1913; President County Medical Society, 1916; President Medical Woman's National Assn. 1922-1924; Councillor International Medical Woman's Assn. Her subject is: "A Contribution to the Study of Women in Medicine". Page 527. Address: Middletown, Connecticut.

## THE BOSTON MEDICAL LIBRARY

### BOSTON MEDICAL HISTORY CLUB

When in the course of the evolution of a civilization sufficient time has elapsed to permit of the valuation of the various factors which have entered into the growth and development of that civilization, students of politics, economics and government begin to survey the facts, appraise their value, discuss their bearing upon one another and the summation of such researches is History. Such investigations are valuable for several reasons. They disclose the currents of thought which have actuated men in their search for a solution of the riddle of life. It throws into high relief the personalities who have contributed to the product under investigation. It supplies suggestions for further development along lines which seem most promising and warns against pitfalls which, because they were not foreseen, have proven disastrous. Besides all this it clothes the subject with an interest that tends to make those who are to benefit all the more concerned that their contribution to the ultimate achievement should be a worthy one and the best that it is possible for them to make.

General interest in Medical History is showing signs of being on the increase. Educators are coming to appreciate its importance in the medical curriculum where it may supply an interest not merely cultural but specifically helpful to the student as he grows older in his work, enabling him to distinguish what is spurious from what is of true worth. Once this interest is planted in his mind it will grow with his years, tinging all his professional endeavors with lights which will infinitely enhance the satisfactions of professional study and practice. The field of Medical History has been as yet but very slightly cultivated. The number of text books which are other than compendious accumulations of data, chronologically arranged, are comparatively few. The medical historian, to date, has had more of a flare for medicine than he has for uncovering the undercurrents of medical and scientific thought and placing them in an historic perspective. There are rich deposits of medical biography and there have been a few who have tilled the field of medical Bibliography, quite intensively. This Library is fairly well stocked with the best there is in these lines. What we wish to encourage is a wider interest in such, on the part of those who as students did not have this interest imparted to them, as well as provide for those who have the advantage of youth and the sources of information which an institution devoted to the collection of such treasures has provided. Medical schools are awakening to the significance of this subject for their students as well as their graduates. Boston with its cultural traditions can ill afford to yield the palm in such a movement to another.

We have in connection with this Library and originated by some of its Officers, a Medical History Club whose activities cover the academic year. Its object is to further an interest in this most important subject and provide for any who desire an outlet for their activities. Local New England Medical History is as full of interest as it is of historic significance in any other line and it is of immense importance that it be brought to the front. Much that is of worthwhile significance for our times in medicine had its birth on this soil and the memory of those who were instrumental in making New England Medical History should not be forgotten. It is hoped that those who are reached by the New England Journal of Medicine and who have an interest in Medical History will keep watch of its notices and join us here, both by their attendance and active membership interest in the Club thereby increasing the usefulness of this live organization, which is capable of supplying entertainment and better still, of contributing to the cultural influence of a profession which is deserving, because of its past record of accomplishment, of the enthusiastic co-öperation of its membership. One of the early meetings this fall will be devoted to setting forth the contributions to the medical progress of New England of a family who for a full century and more, have been conspicuous for their influence in shaping the life, both civic and medical, of that period. That meeting should have not merely a local interest but should draw from all New England. Ample notice of subject, time and place will be supplied by the New England Journal of Medicine.

## MISCELLANY

### VIRGIL PENDLETON GIBNEY MEMORIAL FELLOWSHIP OF THE HOSPITAL FOR RUPTURED AND CRIPPLED

Through the generous contributions of the Alumni and friends of the Hospital for Ruptured and Crippled, a fellowship has been established which will be known as the Virgil Pendleton Gibney Memorial Fellowship.

The income from this fellowship will be approximately fifteen hundred dollars a year; and the incumbent thereof will have the privilege of boarding and residing at the Hospital.

The idea of the fellowship is to afford an opportunity to a man who is well-grounded in general surgery and who has had a certain amount of experience in orthopaedic surgery, to pursue further study in the latter field, especially in that of bone pathology. The incumbent will have every opportunity for clinical study in both the In-door and Out-door Departments of the Hospital. He will have the privilege of carrying on laboratory investigations at the Cornell University Medical College under the direction of the heads of the departments, and also will have an opportunity to study the pathology of bone tumors under the direction of Dr. James Ewing of the Cornell and Memorial Hospital laboratories.

After a period of not exceeding three months, the

incumbent shall decide upon some particular line of study and investigation to which he intends to devote the major portion of his time. At the end of one year, or, of the period during which he has held the fellowship, he shall present to the Committee in Charge, a thesis which will be published as coming from the Hospital for Ruptured and Crippled and the Cornell University Medical College Laboratories, with the approval of the Committee.

The Committee in charge of this fellowship consists of the following:

Mr. William Church Osborn, President of the Board of Managers.
Dr. Samuel Fosdick Jones of Denver, Colorado.
Dr. Eugene H. Pool.
Dr. Royal Whitman.
Dr. Charlton Wallace.
Dr. William B. Coley, Chairman.

Anyone desiring to apply for this fellowship will please communicate with Dr. William B. Coley at the Hospital for Ruptured and Crippled, 321 East 42nd Street, New York, N. Y.

WILLIAM B. COLEY, M.D., *Chairman.*

### THE WORLD'S CHILDREN

PLAYGROUND ACTIVITIES INCREASING

The number of cities reporting to the Playground and Recreation Association of America that they maintain community-recreation programs under leadership increased from 505 in 1922 to 815 in 1927. During the same period the number of paid leaders reported was nearly doubled. Training institutes for employed leaders were reported for 1927 by 146 cities, and the total expenditures reported by 658 cities for that year amounted to more than $32,000,000.—*Notes on Child Welfare Topics Compiled by the U. S. Children's Bureau.*

## CORRESPONDENCE

### THE NORFOLK DISTRICT MEDICAL SOCIETY

September 7, 1928.

THE NEW ENGLAND JOURNAL OF MEDICINE:

The following changes have become necessary in the Norfolk District program for the coming year: The February meeting will be held February 25th and the March meeting March 29th.

Due to the inability of the officers of the Society to obtain reservations for meetings to be held on the last Tuesday of the month as is customary, certain departures will be noticed in the program for the year and the meeting will be held on the date specified, regardless of whether that date is the last Tuesday of the month.

Very truly yours,
F. S. CRUICKSHANK, *Secretary.*

## RECENT DEATHS

**WOODMAN**—DR. WALTER WOODMAN, a graduate of Harvard Medical School in the class of 1883, died at his home in Cambridge, September 4, 1928, aged 76. He was born at Mineral Point, Wisconsin, August 30, 1852, was graduated A.B. at Harvard in 1875, and retired from practice in 1887 when he became a member of the firm of the Tyler Tube and Pipe Company, manufacturers of boiler tubes.

**BACON**—DR. JOSEPH AMBROSE PATRICK BACON, a Fellow of The Massachusetts Medical Society, died at his home in Lawrence, June 5, 1928, aged 61.

He was born at Philadelphia, Pa., January 8, 1867, the son of Joseph A. and Hannah Moore Bacon, was educated at the University of Vermont College of Medicine and at the Baltimore University School of Medicine, taking his M.D. from the latter in 1891. He settled in Lawrence in 1898 and was superintendent of the Lawrence Municipal Hospital. During the World War Dr. Bacon was first lieutenant in the Medical Corps U. S. A. He was a charter member of Lawrence Post 15, American Legion and a member of the Red Men, Knights of Pythias and the Massachusetts Medical Society. The cause of his death was coronary occlusion. He is survived by his widow, Mrs. Isabel E. Haupert Bacon, by a daughter and two brothers and a sister.

## REPORTS AND NOTICES OF MEETINGS

### MEETING OF THE FOUR WESTERN COUNTY MEDICAL SOCIETIES

The Annual Meeting of the Four Western Counties, Hampden, Hampshire, Berkshire and Franklin, was held at the Belchertown State School by invitation of the Trustees on September 12, 1928.

PROGRAM

1:30 p. m. Dinner.

2:45-3:30. (a) Election of Officers. (b) Discussions of Admissions to School. (c) Presentation of some types of mentally deficient children.

4:00 p. m. Certain sports and games were planned.

### NEW ENGLAND SURGICAL SOCIETY TENTH MEETING

New Haven, Conn.

NOVEMBER 9 AND 10, 1928

The Annual Meeting of the New England Surgical Society will be held at New Haven, Conn., on Friday, November 9, and Saturday, November 10.

Reservations should be made as early as possible at the Hotel Taft through Doctor W. E. Hartshorn, 67 Trumbull Street, New Haven, Conn.

All meetings will be held at the New Haven Hospital.

Buffet Luncheons will be served at the New Haven Hospital.

Annual Dinner at the New Haven Lawn Club or the New Haven Country Club, Friday evening, November 9.

Arrangements will be made to entertain the ladies.

*Social Arrangements:*

Yale-Maryland Football Game, November 10, at 2 P. M.

Golf privileges will be available at the New Haven Country Club and at the new Yale Golf Course.

Members who care to remain over Sunday will be shown over the University, or can play Golf at one of the above named Courses.

FRIDAY MORNING, NOVEMBER 9

There will be a symposium on Medical and Surgical Aspects of Large Bowel Affections, followed by a Clinic.

FRIDAY AFTERNOON, NOVEMBER 9

There will be a Literary Program consisting of six diversified papers by members of the Society.

FRIDAY EVENING, NOVEMBER 9

The Annual Dinner. At the Annual Dinner there will be a discussion on the subject, "The Nursing Problem." Discussion will be started by Professor Winslow of Yale. Doctor Bigelow, Commissioner of Health of Massachusetts, and Doctor James Stone.

SATURDAY MORNING, NOVEMBER 10

There will be a symposium on Pelvic Surgery, followed by an Operative Clinic.

SATURDAY NOON, NOVEMBER 10

The Annual Business Meeting will take place at noon. JOHN M. BIRNIE, M.D., *Secretary.*

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## PROGRAM, SIXTH NEW ENGLAND HEALTH INSTITUTE, BURLINGTON, VERMONT, SEPTEMBER 24, 25 AND 26, 1928

PRELIMINARY PROGRAM—SUBJECT TO CHANGE

HEADQUARTERS—CITY HALL, BURLINGTON

Presented by State Health Departments of New England Co-öperating with United States Public Health Service, New England Colleges and Voluntary Health Organizations

*Director*—Charles F. Dalton, M.D., Secretary Vermont Department of Public Health, Burlington, Vermont.

*Program Committee*—H. W. Slocum, F. S. Kent, M.D., C. P. Moat, Nellie M. Jones, R.N.

SCHEDULE OF COURSES NEW ENGLAND HEALTH INSTITUTE

Burlington, Vermont, September 24-26, 1928

Letters in () indicate that additional information follows later in the schedule.

1. *Public Health Administration*

| | 9-10 | 10-11 | 11-12 | 2-3 | 3-4 | 4-5 |
|---|---|---|---|---|---|---|
| Mon. | Registration | | (A) | | | |
| Tue. | | (B) | | | (C) | |
| Wed. | | (D) | | Health Entertainment | | |

2. *Preventable Diseases*

| | | | | | | |
|---|---|---|---|---|---|---|
| Mon. | Registration | | | | (A) | (B) |
| Tues. | | | (C) | (D) | (E) | (F) |
| Wed. | (G) | | | Health Entertainment | | |

3. *Sanitation and Engineering*

| | | | | | |
|---|---|---|---|---|---|
| Mon. | Registration | | | | |
| Tue. | (A) | | (B) | (C) | (C) |
| Wed. | | (D) | | Health Entertainment | |

4. *Tuberculosis*

| | | | | | |
|---|---|---|---|---|---|
| Mon. | Registration | | (A) | (B) | (C) |
| Tue. | (D) | | | | (E) |
| Wed. | | | | Health Entertainment | |

5. *Child Hygiene*

| | | | | | |
|---|---|---|---|---|---|
| Mon. | Registration | | | | (A) |
| Tue. | | (B) | (C) | | |
| Wed. | (D) | | (E) | Health Entertainment | |

6. *Public Health Nursing*

| | | | | | |
|---|---|---|---|---|---|
| Mon. | Registration | | | | (A) |
| Tue. | | (B) | (C) | | |
| Wed. | (D) | (E) | (F) | Health Entertainment | |

7. *Social Work*

| | | | | |
|---|---|---|---|---|
| Mon. | Registration | | (A) | (B) |
| Tue. | (C) | | (D) | |
| Wed. | | | Health Entertainment | |

8. *Mental Hygiene*

| | | | | |
|---|---|---|---|---|
| Mon. | Registration | | | |
| Tue. | | | | (A) |
| Wed. | | (B) | (C) | Health Entertainment |

9. *Industrial Hygiene*

| | | | | |
|---|---|---|---|---|
| Mon. | Registration | | | |
| Tue. | | | (A) | (A) |
| Wed. | (B) | | (C) | Health Entertainment |

10. *Foods, Drugs and Nutrition*

| | | | | | |
|---|---|---|---|---|---|
| Mon. | Registration | | (A) | (B) | (C) |
| Tue. | | (D) | | | |
| Wed. | | | Health Entertainment | | |

I. PUBLIC HEALTH ADMINISTRATION

Chairman: C. F. Kendall, M.D., Commissioner of Health, Augusta, Me.

Mon. 11-12 *a.* Public Health Administration, Howard A. Streeter, M.D., Health Officer, Manchester, N. H.

Tues. 10-11 *b.* The Evaluation of Morbidity Surveys. Herbert L. Lombard, M.D., Massachusetts Department of Public Health.

Tues. 3-4 *c.*

Wed. 10-11 *d.* Subjects and speakers not yet announced.

II. PREVENTABLE DISEASES

Chairman: C. A. Weaver, M.D., Division of Preventable Diseases, State Department of Health, Concord, N. H.

Mon. 3-4 *a.* "Scarlet Fever." Elliott Robinson, M.D., Ph.D., Ass't Director Div. Biologic Laboratories, Dept. Public Health, Mass.

Mon. 4-5 *b.* "Public Health Nursing in Preventable Diseases." Francis P. Denny, M.D., Health Officer, Brookline, Mass. Session combined with Public Health Nursing *a.*

Tues. 11-12 *c.* "Typhoid Fever Control." Filip C. Forsbeck, M.D., Epidemiologist, Mass. Dept. Public Health.

Tues. 2-3 *d.* "Syphilis." Albert Pfeiffer, M.D., Medical Division Social Hygiene, New York Dept. Public Health, Albany, N. Y.

Tues. 3-4 *e.* "Gonorrhea in the Female." Walter M. Brunet, M.D., Consultant Division Medical Measures, American Social Hygiene Ass'n, New York City.

Tues. 4-5 *f.* "Anterior Poliomyelitis." W. Lloyd Aycock, M.D., Vermont Dept. Public Health, and Harvard Infantile Paralysis Commission.

Wed. 9-10 *g.* "Cancer." P. E. McSweeney, M.D., Chairman Vermont Branch Society for Control of Cancer.

III. SANITATION AND ENGINEERING

Chairman: Chas. D. Howard, S.B., Chief, Division of Chemistry and Sanitation N. H. State Board of Health, Concord, N. H.

Tues. 9-10 *a*. "Sanitation of Flooded Areas." Prof. J. W. Votey, C.E., Sc.D., Dean of the College of Engineering, University of Vermont. Sanitary Engineer, State Dept. of Public Health, Burlington, Vermont.

Tues. 11-12 *b*. "The Septic Tank as a Transformer of Sewage." Prof. Robert Fletcher, Ph.D., C.E., Hanover, N. H., Pres. N. H. State Board of Health, Formerly Dean, Thayer School of Engineering, Dartmouth College.

Tues. 2-4 *c*. "Dust Control in Industry." Theodore Hatch, Instructor in Sanitary Engineering, Harvard University, Cambridge, Mass. In his talk, Mr. Hatch will include a discussion of the hazards attendant upon the granite and marble cutting industries.

This session will be combined with the section on Industrial Hygiene.

Wed. 10-11 *d*. "Sanitary Hazards in Water Distribution." E. Sherman Chase, Sanitary Engineer, of Metcalf and Eddy, Statler Building, Boston, Mass. Mr. Chase in his address will give the subject of emergency intakes and industrial secondary cross-connections on public water systems special treatment.

### IV. Tuberculosis

Chairman: B. D. Merrill, M.D., Dover-Foxcroft, Me.

Mon. 11-12 *a*. "Tuberculosis Nursing in Rural Territory." Marion Garland, R.N., Laconia, N. H.

Mon. 2-3 *b*. "Physical Inspection of School Children in Rural Communities." James N. Pringle, Deputy Commissioner of Education of the State of New Hampshire.

Mon. 4-5 *c*. Subject not yet announced.

Tues. 9-10 *d*. "Childhood Tuberculosis." Dr. Cole B. Gibson, M.D., Supt. Meriden, Conn., State Tuberculosis Sanatorium. Discussion led by Robt. B. Kerr, M.D., of New Hampshire.

Tues. 4-5 *e*. Session combined with Child Hygiene *a*.

### V. Child Hygiene

Chairman: Merrill Champion, M.D., Director, Division of Hygiene, State Department of Public Health, Boston, Mass.

Mon. 3-4 *a*. Round Table Discussion on Public Health Education. (This will be combined with the Tuberculosis Division.) Merrill Champion, M.D., Director, Division of Hygiene, State Dept. of Public Health, Boston, Mass.

Tues. 10-11 *b*. Talk on Breast Feeding. Not yet announced.

Tues. 11-12 *c*. "The Health Supervision of the Preschool Child" (with a discussion of community response). C. K. Johnson, M.D., Burlington, Vt.

Wed. 9-10 *d*. "The Nurse and the Nutrition Program." Not yet announced.

Wed. 11-12 *e*. "The Correction of Dental Defects—a Community Responsibility." Miss Eleanor B. Gallinger, Consultant in Dental Hygiene, Massachusetts State Department of Public Health.

### VI. Public Health Nursing

Chairman: Elizabeth P. Van Patten, R.N., Visiting Nurse Ass'n, New Haven, Conn.

Mon. 4-5 *a*. Combined session with Preventable Disease *b*.

Tues. 10-11 *b*. General Program of Public Health Nursing. Not yet announced.

Tues. 11-12 *c*. "Social Problems Met in the Course of Health Work, Their Types, Symptoms, and Methods of Handling." (Combined session with section on Social Work *d*.) Not yet announced.

Wed. 9-10 *d*. Combined session with Child Hygiene.

Wed. 10-11 *e*. "Poliomyelitis, The Nursing Care in Acute Stage and the After-Care." Lillian E. Kron, R.N., Director, "After-Care" for Poliomyelitis, Dept. of Public Health, Burlington, Vt.

Wed. 11-12 *f*. "Public Health Nurse and the Home Care of the Diabetic." Not yet announced.

### VII. Social Work

Chairman: H. F. Perkins, Ph.D., Professor of Zoölogy, University of Vermont.

Mon. 2-3 *a*. "Social Work and Its Relations to Delinquency—Human Salvage." Not yet announced.

Mon. 3-4 *b*. "The Diverting of Delinquent Trends." Not yet announced.

Tues. 9-10 *c*. "A Practical Program for Juvenile Delinquents." Not yet announced.

Tues. 11-12 *d*. Combined Session with Public Health Nursing *c*.

### VIII. Mental Hygiene

Chairman: Stanley H. Osborne, M.D., Commissioner of Public Health, Hartford, Conn.

Tues. 4-5 *a*. "The Mental Health of the Community." William D. Terhune, M.D., Stockbridge, Mass.

Wed. 10-11 *b*. Not yet announced.

Wed. 11-12 *c*. Not yet announced.

### IX. Industrial Hygiene

Chairman: Harold W. Stevens, M.D., Jordan Marsh Company, Boston, Mass.

Tues. 2-4 *a*. Combined session with Sanitation and Engineering *c*.

Wed. 9-10 *b*. "The Private Physician's Part in Industry." Symposium by Stanley H. Osborne, M.D., Commissioner of Public Health, Hartford, Conn., and Albert Gray, M.D., Chief Division of Occupational Diseases Connecticut Department of Public Health.

Wed. 11-12 *c*. "Food and Nutrition for Workers in Industry." Charles W. McClure, M.D., Boston, Mass.

### X. Foods, Drugs and Nutrition

Chairman: Herman C. Lythgoe, M.D., Director, Division of Food and Drugs, State Department of Public Health, Boston, Mass.

Mon. 11-12 *a*. Subject to be announced. Allan Winter Rowe, M.D., Evans Memorial Hospital.

Mon. 2-3 *b*. Subject to be announced. W. S. Frisbie, U. S. Department of Agriculture.

Mon. 4-5 *c*. "The Work of the Food and Drugs Division of the Mass. Dept. of Public Health." Herman C. Lythgoe, M.D., Dept. of Health, Boston, Mass.

Tues. 10-11 *d*. Not yet announced.

## *SPECIAL NOTICES*

### Hotel Accommodations and Rates

*New Sherwood Hotel:*

| | |
|---|---|
| Single room without bath, per day | $2.00 |
| Double room without bath, per day | $3.00 |
| Single room with bath, per day | $2.50 |
| Double room with bath, per day | $4.00 |

*Hotel Vermont:*

Rooms without bath occupied by one person, per day..... $2.50
Rooms without bath occupied by two persons, per day..... $4.00
Rooms with private bath occupied by one person, per day..... $3.50
Rooms with private bath occupied by two persons, per day..... $6.00
Rooms with twin beds and bath $7.00 and $8.00 according to size and location.

*Hotel Van Ness:*

Rooms without bath occupied by one person, per day..... $2.00
Rooms without bath occupied by two persons, per day..... $3.50
Rooms with private bath occupied by one person, per day..... $3.00
Rooms with private bath occupied by two persons, per day..... $5.00
Rooms with twin beds and bath, $6.00 to $8.00 per day according to size and location.

Guests are requested to make reservations directly with the hotel and as early as possible. All hotels are within convenient distance of meeting place.

For information in regard to rooms in private homes, write the Chamber of Commerce, Burlington, Vermont.

New England Health Institute executive committee special luncheon meeting, Hotel Vermont, Tuesday noon. Christmas seal breakfast, Hotel Vermont, Tuesday morning at 7:45.

Plans are being made for an unique health entertainment to be followed by auto trips around Burlington for Wednesday afternoon. Let's stay and get acquainted.

## CLINICAL CONGRESS OF PHYSICAL THERAPY AND SEVENTH ANNUAL MEETING OF THE AMERICAN COLLEGE OF PHYSICAL THERAPY

Announcement is made of the third clinical Congress on Physical Therapy in conjunction with the seventh annual meeting of the American College of Physical Therapy, to be held at the Hotel Stevens, Chicago, October 8th to 13th, 1928. For the past year plans have been under way to make this 1928 Congress the most interesting one ever conducted and one which will be difficult to surpass in the future. So many novel and attractive features have been injected in the six day program that no physician, whether he is now doing physical therapy or whether he plans to do it later, can possibly afford to absent himself from this scientific gathering.

The scientific addresses to be presented are of vital importance to the medical profession and will come from leading European and American authorities on the basic and practical phases of physical therapeutics. Symposiums on Cancer and Tuberculosis, the newest scientific information in these fields should attract physicians from all sections, for no two problems in the field of medicine require more thorough and extensive research and elaboration than these. Sectional meetings in *medicine, surgery,* and allied branches, and in eye, ear, nose, throat and oral surgery will be of interest to specialists in their respective fields, and for those who are new in physical therapy, special instruction classes in the physics and practical application of the various physical agents have been arranged.

Dr. Carl Sonne of the Finsen Medical Light Institute, Copenhagen, Denmark; Cav. Prof. Dr. Donato de Francesco of Venice, Italy; and Dr. A. R. Friel of London, England, will expound the results of their personal investigations in their respective specialties, while over one hundred leading physicians and teachers from all parts of North America will complete a program that cannot help prove inviting to every worker in physical therapy.

The technical and scientific exhibits will furnish an array of material that you will want to see. The demonstration clinics, the group conferences, the clinical addresses, the round table talks and the hospital clinics make up other parts of the program. No expense has been spared to bring together the best talent available, so that this event should prove an unusual scientific forum for the discussion of diathermy, light galvanism, X-ray, radium, massage, sinusoidalism, therapeutic exercises, etc., etc.

Physicians, their non-medical assistants and technicians, and hospital executives properly vouched for, are invited to attend all sessions for which only a nominal registration fee will be charged.

Write for program, registration card and other information now, as early registration by mail is urgently solicited because the instruction classes are limited.

Suite 820—30 North Michigan Avenue, Chicago, Illinois.

## THE CLINICAL CONGRESS OF THE AMERICAN COLLEGE OF SURGEONS

The Eighteenth Annual Clinical Congress of the American College of Surgeons will be held in Boston October 8-12.

## SOCIETY MEETINGS

**September 10-14**—American Electrotherapeutic Association. Entire program appears on page 499 of September 6 issue.

**September 18, 19, 20**—Fourth Clinical Congress, Connecticut State Medical Society. For detailed notice see page 394, issue of August 23.

**September 24-28**—Sixth Conference of the International Union Against Tuberculosis. For complete notice see page 349, issue of August 16.

**September 24-25-26**—Program of the Sixth New England Health Institute, Burlington, Vermont. For complete notice see page 543, this issue.

**October 1-12**—The Graduate Fortnight of the New York Academy of Medicine. For complete notice see page 396, issue of August 23.

**October 8-12**—Clinical Congress of the American College of Surgeons. For complete notice see above.

**October 8-13**—Clinical Congress of Physical Therapy and Seventh Annual Meeting American College of Physical Therapy. Complete notice appears elsewhere on this page.

**October 15-19**—Interstate Post Graduate Association. Complete notice on page 1025, issue of June 28.

**November 9-10**—New England Surgical Society, Tenth Meeting. Complete notice appears on page 542.

**December 3-7**—Radiological Society Convention. Detailed notice appears on page 712, issue of May 17.

### DISTRICT MEDICAL SOCIETIES

#### Barnstable District Medical Society

Schedule of Meetings: November 1, 1928, February 7, 1929, May 2, 1929.

#### Berkshire District Medical Society

The especial features of the October meeting will be addresses by Dr. George Crile of Cleveland, Dr. Emil Novak of Johns Hopkins, Dr. Willis Campbell of Memphis, Tennessee, and Dr. Thomas Ordway of Albany, N. Y.

A complete program will be published later.

HUGH J. DOWNEY, Secretary.

### Bristol North District Medical Society

**September 20**—Fall meeting will be held at the Bristol County Tuberculosis Hospital, Oak Hill Avenue, Attleboro, at 2 P. M.
**April 18, 1929**—Spring meeting.

### Bristol South District Medical Society

Meetings will be held November 7, 1928, and May 2, 1929. Complete notices will appear later.

### Essex North District Medical Society

**October 17, 1928** (Wednesday afternoon), at 2 P. M.—A joint meeting with Middlesex East and North, and Essex South will be held at Essex Sanatorium at Middleton. (Telephone Danvers 300-W.)

**November 1, 1928** (Thursday)—Censors meet at Hotel Bartlett, 95 Main Street, Haverhill (Tel. 3430), at 2 P. M.

**January 2, 1929** (Wednesday)—Semi-annual meeting at Haverhill, at 12:30 P. M.

**May 1, 1929** (Wednesday)—Annual meeting at Lawrence, at 12:30 P. M.

**May 2, 1929** (Thursday)—Censors meet at Hotel Bartlett, 95 Main Street, Haverhill, at 2 P. M. (Tel. 3430.)

### Middlesex East District Medical Society

The following schedule of meetings has been arranged for the coming year:
**September 12**—Winchester Country Club.
**October 17**—Middleton. (Joint meeting with Essex North and South and Middlesex North.)
**November 14**—Woburn.
**January 16**—Wakefield.
**March**—Reading.
**May**—Melrose.

Subjects and speakers to be arranged by committees in each city or town.

### Middlesex North Medical Society

**October 17**—A combined meeting with Essex North and South.
The winter meeting will be held the last Wednesday in January.
The annual meeting will be held the last Wednesday in April.

### Norfolk District Medical Society

Below are the proposed meetings of the Norfolk District Medical Society for the 1928-29 Season. The schedule below will be adhered to as strictly as possible. The carrying out of the proposed plan will, of course, depend upon the acceptances of invitations extended to the speakers. Minor changes may be necessary.

**October 30**—Pondville Hospital. Dr. Lyman F. Jones, Superintendent. Inspection, 4 P. M.; Business Meeting at 5:30; Papers by the Staff; Collation.

**November 21**—Boston Medical Library. In combination with Suffolk District and Middlesex East District Societies. Subject, Physiotherapy—Dr. F. B. Granger.

**January 29**—Roxbury Masonic Temple. Subject, Treatment of Varicose Veins by the Injection Method—Dr. E. E. O'Neil. Dr. Homans will open the discussion.

**February 25**—Roxbury Masonic Temple. Dr. W. R. Ohler. Subject to be announced. Discussion to be opened by Dr. A. A. Hornor.

**March 29**—Roxbury Masonic Temple. Subject and speakers to be announced.

**May, 1929**—Annual meeting program to be announced.

The Censors of the Society meet November 8, 1928, and May 9, 1929, at the Roxbury Masonic Temple, Warren Street, Roxbury, at 4 P. M., for the examination of candidates.

## BOOK REVIEWS

*Strabismus, Its Etiology and Treatment.* By OSCAR WILKINSON, A.M., M.D., D.Sc. A book of 230 pages with 120 illustrations. C. V. Mosby Company, 1927.

In his preface, Wilkinson states that his book "has been written in the interest of the cross-eyed child". The importance of an early ocular investigation of the children of strabismic parents, and of early treatment of the cross-eyed child is a matter not fully realized by most parents or by many practicing physicians. Delay in recognition and therefore inappropriate treatment of cross-eye results in visual defects, and eventually in stamping an inferiority complex upon the unfortunate child. Wilkinson has fulfilled his stated purpose admirably with a book that with its first two chapters will interest the average layman, and throughout its entire extent will instruct the average physician. The text is enhanced with numerous illustrations, many of which are in color.

The first chapter deals with the history of studies upon strabismus. The second chapter treats of various theories of the etiology of strabismus and the author is generous in quotations from the leading thinkers along these lines. Subsequent chapters discuss the anatomy and the physiology of the oculomotor mechanism, and the study and treatment, non-operative and operative, of the different types of strabismus. The work is one which merits a cordial reception.

## BOOKS RECEIVED FOR REVIEW

*L'Exploration Radiologique en Gynecologie.* Edited by Claude Beclere. Published by Masson et Cie, Editeurs. 173 Pages.

*The Surgical Operations on President Cleveland in 1893.* Edited by William W. Keen, M.D. Published by J. B. Lippincott Company. 251 Pages.

*R. T. H. Laennec: A Memoir.* Edited by Dr. Gerald B. Webb. Published by Paul B. Hoeber, Inc. 146 Pages.

*Manuel de Bacteriologie Medicale.* Published by Masson et Cie. 551 Pages.

*Studies from the Rockefeller Institute for Medical Research.* Reprints Volume 64. Published by the Rockefeller Institute for Medical Research. 640 Pages.

*Prescribing Occupational Therapy.* Edited by William Rush Dunton, Jr. Published by Charles C. Thomas. 142 Pages.

*Nouveau Precis de Bacteriologie.* By G. Delater and Ch. Grandclaude. Edited by Gauthier-Villars et Cie. 124 Pages.

*The Opium Problem.* Edited by Charles E. Terry, M.D., and Mildred Pellens. Published by the Committee on Drug Addictions in collaboration with Bureau of Social Hygiene, Inc. 1042 Pages.

*Boston City Hospital Training School for Nurses.* Edited by Mary M. Riddle. Published by University Press. 203 Pages.

*Preventive Medicine* by Mark F. Boyd. Published by W. B. Saunders Company. 475 Pages.

*An Introduction to Experimental Pharmacology* by Torald Sollmann, and Paul J. Hanzlik. Published by W. B. Saunders Company. 321 Pages.

*Acute Aplastic Anaemia. Its Relation to a Liver Hormone. Report and Observations in Case Treated by Injections of Liver Extract* by A. Hayes Smith. Published by H. K. Lewis & Co., Ltd. VII and 80 Pages.

*Bronchial Asthma* by Harry L. Alexander. Published by Lea & Febiger. 161 Pages.

*Fractures and Dislocations* by Kellogg Speed. Published by Lea & Febiger. 952 Pages.

*United States Naval Medical Bulletin.* Published by Bureau of Medicine and Surgery. 783 Pages.

The JOURNAL does not publish the price of books received for review because of Postal regulations. Requests for this information addressed to the JOURNAL office will receive early attention.